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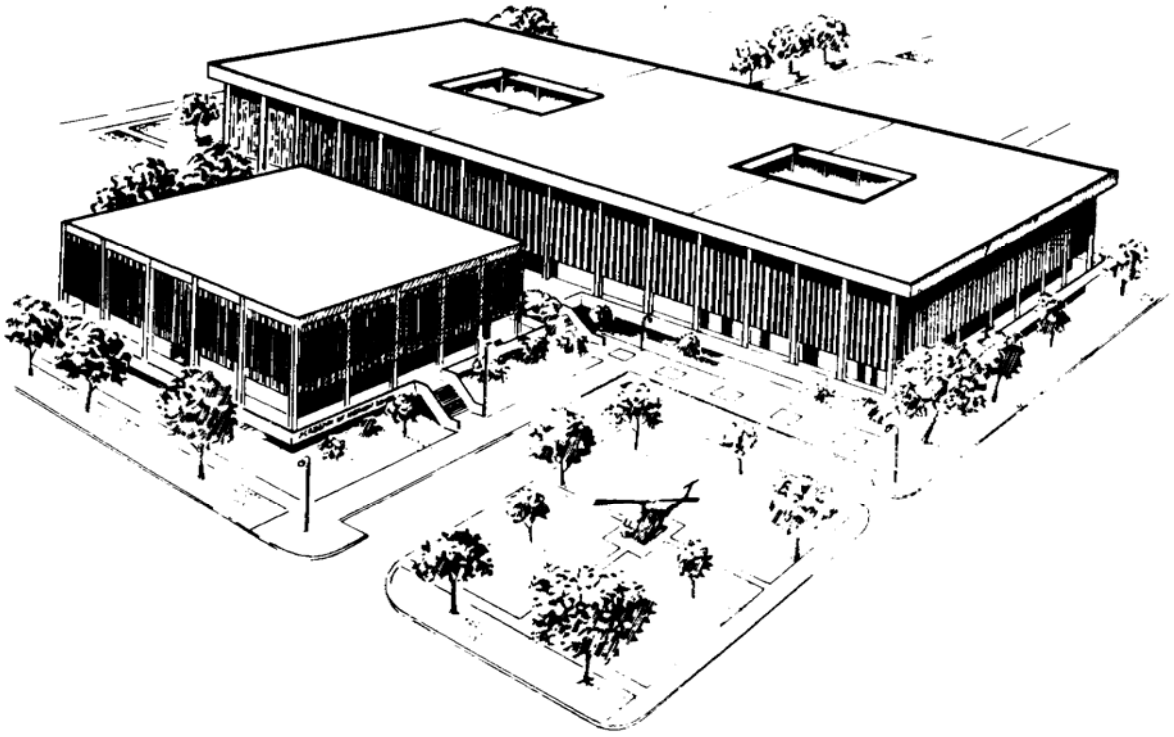
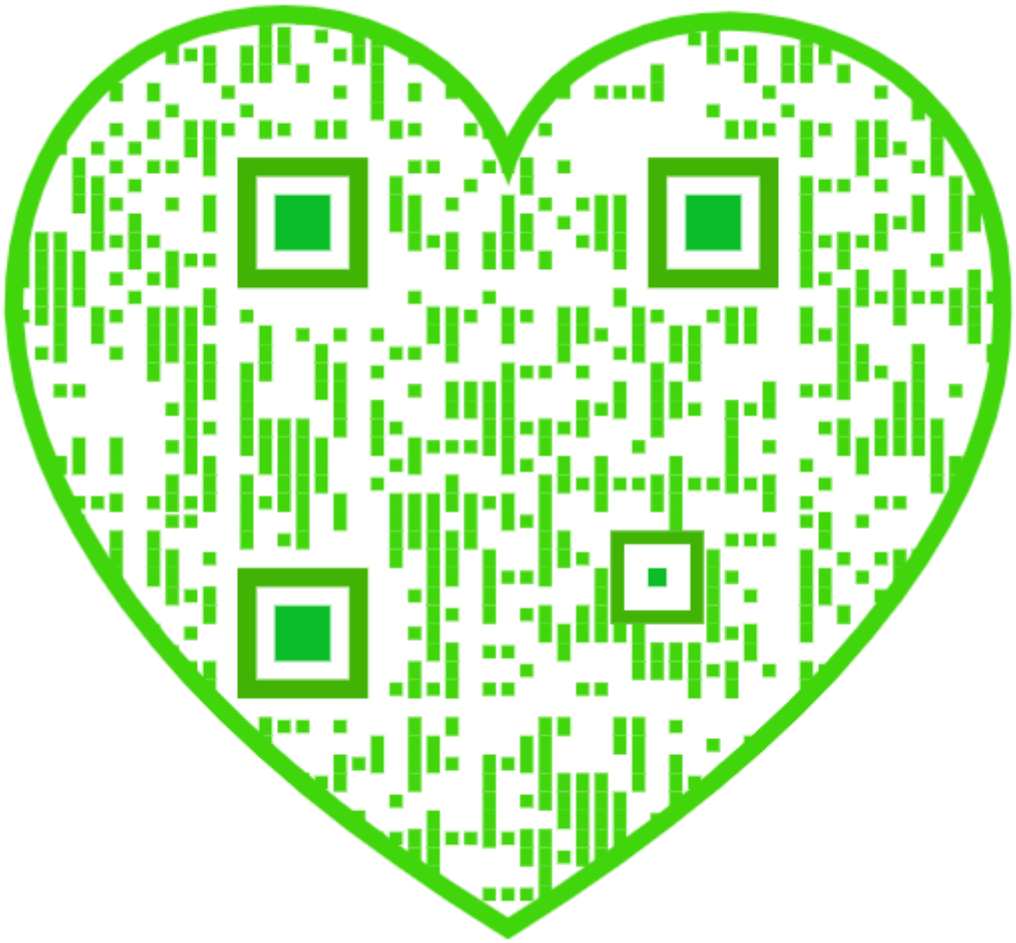
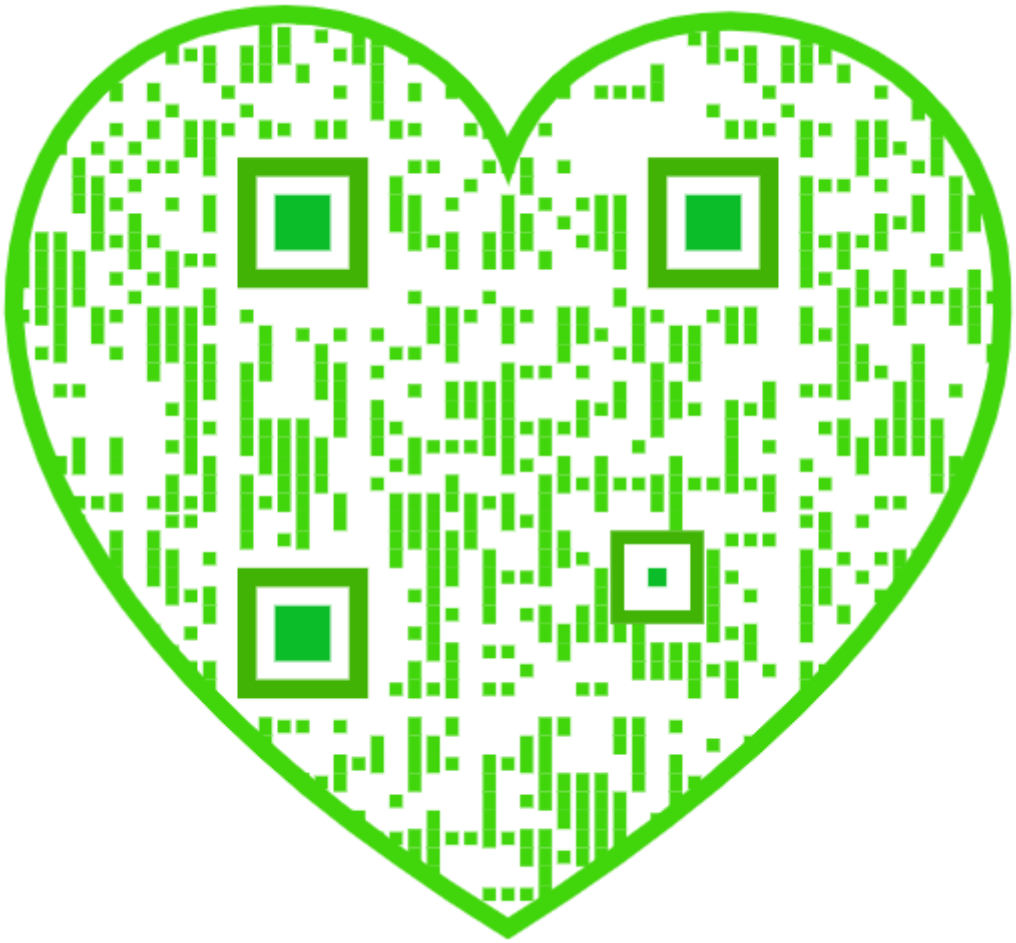


THERAPEUTICS III

SUBCOURSE MD0806 EDITION 200





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When used in this publication, words such as "he," "him," "his," and "men" are intended to include both the masculine and feminine genders, unless specifically stated otherwise or when obvious in context.

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CORRESPONDENCE COURSE OF
U.S. ARMY MEDICAL DEPARTMENT CENTER AND SCHOOL

SUBCOURSE MD0806

THERAPEUTICS III

INTRODUCTION

Drugs that act upon the respiratory system, cardiovascular system, or urinary system are frequently dispensed in both military and civilian pharmacies. This is because conditions that affect these systems (that is, hypertension affecting the cardiovascular system) affect many people. Consequently, it is imperative that you have an understanding of these systems and the drugs that act on them.

As with MD0804 (Therapeutics I) and MD0805 (Therapeutics II), anatomy, physiology, and pharmacology are presented in a combined perspective. This is done to help you to understand and remember the actions, uses, side effects, and patient warnings associated with the drugs included in these lessons.

You should remember that this subcourse is not intended to replace accepted references in anatomy, physiology, or pharmacology. Instead, it is designed to help you gain a background in these areas so that you may continue learning in a self-directed manner. You are encouraged to read pertinent journals, study pharmacology texts, and talk to fellow health-care professionals in order to learn more about the topics presented in this subcourse.

This subcourse consists of 9 lessons as follows:

Lesson 1. The Respiratory System and Respiratory System Drugs.

Lesson 2. The Human Cardiovascular and Lymphatic Systems.

Lesson 3. Cardiac Drugs.

Lesson 4. Vasodilator Drugs.

Lesson 5. Drugs Acting on the Hematopoietic System.

Lesson 6. The Human Urogenital Systems.

Lesson 7. Antihypertensive Drugs.

Lesson 8. Diuretic and Antidiuretic Agents.

Lesson 9. Toxicology and Poison Control.

--Complete the subcourse lesson by lesson. After completing each lesson, work the exercises at the end of the lesson

--After completing each set of lesson exercises, compare your answers with those on the solution sheet that follows the exercises. If you have answered an exercise incorrectly, check the reference cited after the answer on the solution sheet to determine why your response was not the correct one.

Credit Awarded:

Upon successful completion of the examination for this subcourse, you will be awarded 14 credit hours.

To receive credit hours, you must be officially enrolled and complete an examination furnished by the Nonresident Instruction Section at Fort Sam Houston, Texas.

You can enroll by going to the web site http://atrrs.army.mil and enrolling under "Self Development" (School Code 555).

LESSON ASSIGNMENT

SUBCOURSE MD0806	Therapeutics III.
LESSON 1	The Respiratory System and Respiratory System Drugs.
LESSON ASSIGNMENT	Paragraphs 1-1--1-20.
LESSON OBJECTIVES	After you finish this lesson you should be able to:

1-1. Given a group of statements and one of the following terms: respiration, external respiration, or internal respiration, select the statement which best defines the given term.

1-2. Given a diagram of the human respiratory system and a list of names of the parts of the human respiratory system, match the name of its part with its proper location.

1-3. Given the name of one of the components of the human respiratory system and a group of statements, select the statement that best describes that component or its function.

1-4. From a group of statements, select the statement which best describes either costal (thoracic) or diaphragmatic (abdominal) breathing.

1-5. Given the name of a condition affecting the respiratory system and a group of statements, select the statement that best describes the given condition.

1-6. Given the name of a type of respiratory system drug (that is, antitussive agent) and a group of statements, select the statement that best describes that type of agent.

1-7. Given the trade or generic name of a respiratory system drug and a group of indications, uses, side effects, or patient precautionary statements, select the indication(s), use(s), side effect(s), or patient precautionary statement(s) for the given drug name.

1-8. Given the trade or generic name of a respiratory system drug and a group of trade and/or generic names, select the given drug's corresponding trade or generic name.

SUGGESTION

After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 1

THE RESPIRATORY SYSTEM AND RESPIRATORY SYSTEM DRUGS

Section I. THE RESPIRATORY SYSTEM

1-1. INTRODUCTION

a. **Respiration.** Respiration is the exchange of gases between the atmosphere and the cells of the body. It is a physiological process. There are two types of respiration-external and internal. External respiration is the exchange of gases between the air in the lungs and blood. Internal respiration is the exchange of gases between the blood and the individual cells of the body.

b. **Breathing**. Breathing is the process that moves air into and out of the lungs. It is a mechanical process. There are two types of breathing in humans--costal (thoracic) and diaphragmatic (abdominal). In costal breathing, the major structure causing the movement of the air is the rib cage. In diaphragmatic breathing, interaction between the diaphragm and the abdominal wall causes the air to move into and out of the lungs.

1-2. COMPONENTS AND SUBDIVISIONS OF THE HUMAN RESPIRATORY SYSTEM

NOTE: See figure 1-1 for an illustration of the human respiratory system.

a. **Components**. The components of the human respiratory system consist of air passageways and two lungs. Air moves from the outside of the body into tiny sacs in the lungs called alveoli (pronounced al-VE-oh-lie).

b. **Main Subdivisions**. The main subdivisions of the respiratory system may be identified by their relationship to the voice box or larynx. Thus, the main subdivisions are as given in table 1-1.

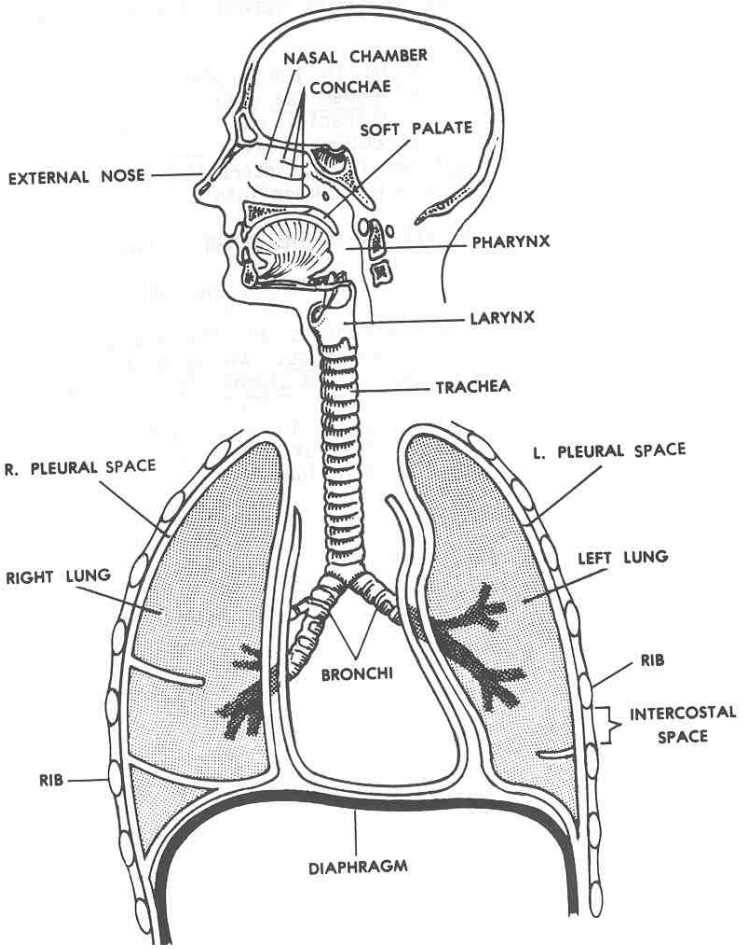


Figure 1-1. The human respiratory system.

SUBDIVISION	FUNCTION
(1) SUPRALARYNGEAL STRUCTURES (su-prah-lah-RIN-je-al)	cleanse, warm, moisten, and test inflowing air
(2) LARYNX (voice-box) (LARE-inks)	controls the volume of inflowing air; produces selected pitch (vibration frequency) in the moving column of air
(3) INFRALARYNGEAL STRUCTURES (in-frah-lah-RIN-je-al)	distribute air to the alveoli of the lung where the actual external respiration takes place

Table 1-1. Major subdivisions of the human respiratory system.

1-3. SUPRALARYNGEAL STRUCTURES

Supralaryngeal structures are shown in figure 1-2.

a. **External Nose**. The external nose is the portion projecting from the face. Primarily cartilages support it. It has a midline divider called the nasal septum, which extends from the internal nose. Paired openings (nostrils lead to paired spaces (vestibules). Guard hairs in the nostrils filter inflowing air.

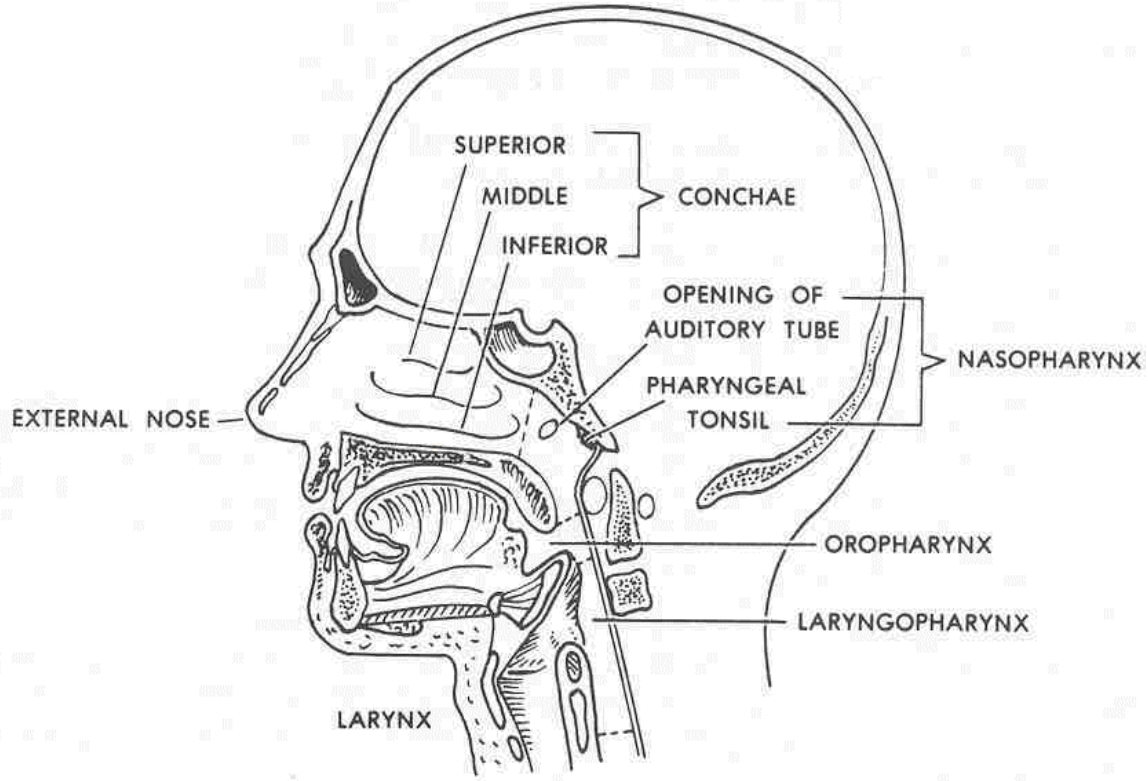


Figure 1-2. Supralaryngeal structures.

b. **Nasal Chambers (Internal Nose)**. Behind each vestibule of the external nose is a nasal chamber. The two nasal chambers together form the internal nose. These chambers too are separated by the nasal septum.

(1) Mucoperiosteum. The walls of the nasal chambers are lined with a thick mucous-type membrane known as the mucoperiosteum. It has a ciliated epithelial surface and a rich blood supply, which provides warmth and moisture. At times, it may become quite swollen.

CILIATED = Provided with cilia (hair like projections that move fluids to the rear)

(2) Conchae. The lateral wall of each chamber has three scroll-like extensions into the nasal chamber, which help to increase the surface area exposed to the inflowing air. These scroll-like extensions are known as conchae.

CONCHA = sea shell
CONCHA (singular)
CONCHAE (plural), (pronounced KON -kah)

(3) Olfactory epithelium. The sense of smell is because of special nerve endings located in the upper areas of the nasal chambers. The epithelium containing the sensory endings is known as the olfactory epithelium.

(4) Paranasal sinuses. There are air "cells" or cavities in the skull known as paranasal sinuses. The paranasal sinuses are connected with the nasal chambers and are lined with the same ciliated mucoperiosteum. Thus, these sinuses are extensions of the nasal chambers into the skull bones. For this reason, they are known as paranasal sinuses.

c. **Pharynx.** The pharynx (FAIR-inks) is the common posterior space for the respiratory and digestive systems.

(1) Nasopharynx. That portion of the pharynx specifically related to the respiratory system is the nasopharynx. It is the portion of the pharynx above the soft palate. The two posterior openings (nares) of the nasal chambers lead into the single space of the nasopharynx. The auditory (eustachian) tubes also open into the nasopharynx. The auditory tubes connect the nasopharynx with the middle ears (to equalize the pressure between the outside and inside of the eardrum). Lying in the upper posterior wall of the nasopharynx are the pharyngeal tonsils (adenoids). The soft palate floor of the nasopharynx is a trap door that closes off the upper respiratory passageways during swallowing.

(2) Oropharynx. The portion of the pharynx closely related to the digestive system is the oropharynx. It is the portion of the pharynx below the soft palate and above the upper edge of the epiglottis. (The epiglottis is the flap that prevents food from entering the larynx (discussed below) during swallowing.)

(3) Laryngopharynx. That portion of the pharynx that is common to the respiratory a digestive systems is the laryngopharynx. It is the portion of the pharynx below the upper edge of the epiglottis. Thus, the digestive and respiratory systems lead into it from above, and lead off from it below.

1-4. LARYNX

The larynx, also called the Adam's apple or voice box, connects the pharynx with the trachea. The larynx, located in the anterior neck region, has a box-like shape. See figure 1-3 for an illustration. Since the voice box of the male becomes larger and heavier during puberty, the voice deepens. The adult male's voice box tends to be located lower in the neck; in the female, the larynx remains higher and smaller and the voice is of a higher pitch.

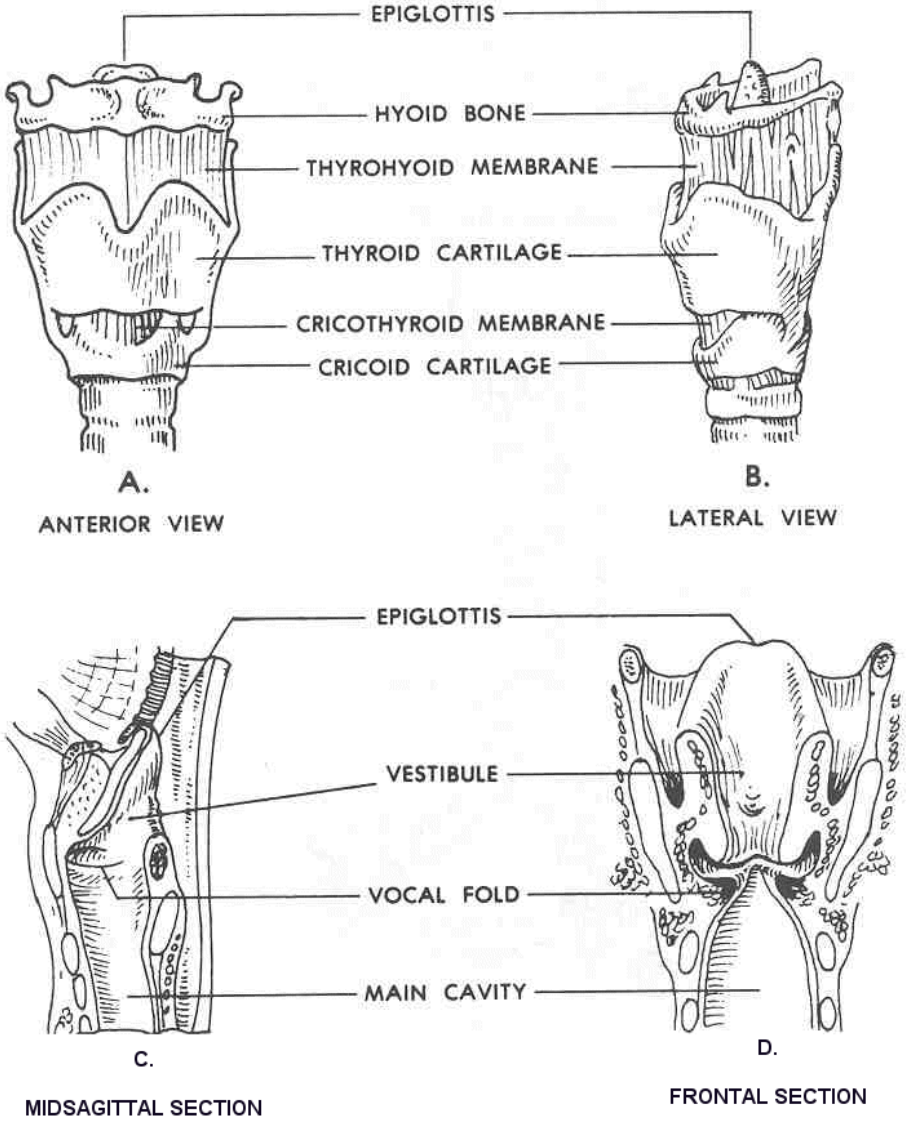


Figure 1-3. The larynx.

a. **Parts and Spaces**. The larynx has a vestibule (“entrance hallway”) that can be covered over by the epiglottis. The glottis itself is the hole between the vocal cords. Through the glottis, air passes from the vestibule into the main chamber of the larynx (below the cords) and then into the trachea. The skeleton of the larynx is made up of a series of carti1ages.

b. **Muscles.** The larynx serves two functions and there are two sets of muscles--one for each function.

(1) One set controls the size of the glottis. Thus, it regulates the volume of air passing through the trachea.

(2) The other set controls the tension of the vocal cords. Thus, it produces vibrations of selected frequencies (variations in pitch) of the moving air to be used in the process of speaking.

1-5. INFRALARYNGEAL STRUCTURES

a. **Trachea and Bronchi.** The respiratory tree (figure 1-4) is the set of tubular structures that carry the air from the larynx to the alveoli of the lungs. Looking at a person UPSIDE DOWN, the trachea is the trunk of the tree and the bronchi are the branches. These tubular parts are held open (made patent) by rings of cartilage. Their lining is ciliated to remove mucus and other materials that get into the passageway.

b. **Alveoli.** The alveoli (alveolus, singular) are tiny spherical (balloon-like) sacs that are connected to the larger tubes of the lungs by tiny tubes known as alveolar ducts and bronchioles. The alveoli are so small that there are millions in the adult lungs. This very small size produces a maximum surface area through which external respiration takes place. External respiration is the actual exchange of gases between the air in the alveolar spaces and the adjacent blood capillaries through their walls.

c. **Lungs**. A lung is an individual organ composed of tubular structures and alveoli, bound together by fibrous connective tissue (FCT). In the human, there are two lungs, right and left. Each lung is supplied by a primary or main stem bronchus leading off from the trachea. The right lung is larger in volume than the left lung. The left lung must leave room for the heart. The right lung is divided into 3 pulmonary lobes (upper, middle and lower) and 10 bronchopulmonary segments (2 + 3 + 5). The left lung is divided into 2 pulmonary lobes upper and lower) and 8 bronchopulmonary segments (4 + 4). A pulmonary lobe is a major subdivision of a lung marked by fissures (deep folds. Each lobe is further partitioned into bronchopulmonary segments. Each lobe is supplied by a secondary or lobar bronchus. A tertiary or segmental bronchus, a branch of the lobar bronchus supplies each segment.

d. **Pleural Cavities.** Each serous cavity has inner and outer membranes. In the case of the lungs, the inner membrane is known as the visceral pleura which very closely cover the surface of the lungs. The outer membrane is known as the parietal pleura and forms the outer wall of the space. The pleural spaces are the potential spaces between the inner and outer membranes. The opening between the pleural layers contains a slick fluid called pleural fluid. The pleural fluid serves as a lubricant and allows the lungs to move freely with a minimum of friction.

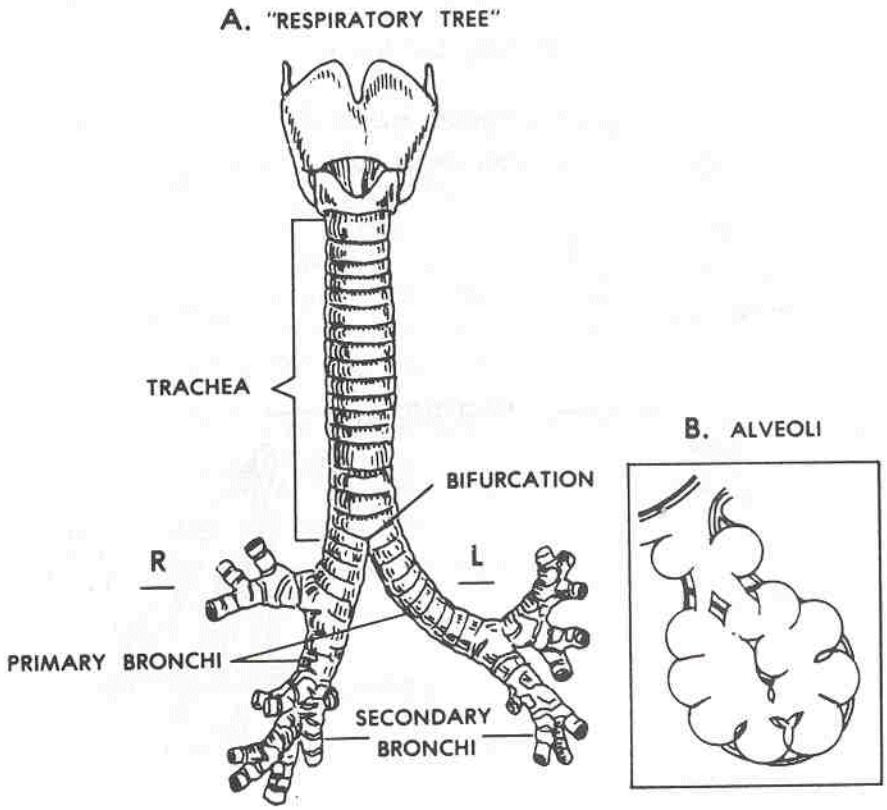


Figure 1-4. Infralaryngeal structures.

Section II. BREATHING AND BREATHING MECHANISMS IN HUMANS

1-6. INTRODUCTION

a. Boyle's law tells us that as the volume (V) of a gas-filled container increases, the pressure (P) inside decreases, and that as the volume (V) of a closed container decreases, the pressure (P) inside increases. When two connected spaces of air have different pressures, the air moves from the space with greater pressure to the one with lesser pressure. In regard to breathing, we can consider the air pressure around the human body to be constant. The pressure inside the lungs may be greater or less than the pressure outside the body. Thus, a greater internal pressure causes air to flow out; a greater external pressure causes air to flow in.

b. We can compare the human trunk to a hollow cylinder. This cylinder is divided into upper and lower cavities by the diaphragm. The upper is the thoracic cavity and is essentially gas-filled. The lower is the abdominopelvic cavity and is essentially water-filled.

1-7. COSTAL (THORACIC) BREATHING

a. **Inhalation**. Muscles attached to the thoracic cage raise the rib cage. A typical rib might be compared to a bucket handle, attached at one end to the sternum (breastbone) and at the other end to the vertebral column. The "bucket handle" is lifted by the overall movement upward and outward of the rib cage. These movements increase the thoracic diameters from right to left (transverse) and from front to back (A-P). Thus, the intrathoracic volume increases. Recalling Boyle's law, the increase in volume (of the chest cavity) leads to a decrease in pressure. The air-pressure outside the body then forces air into the lungs and inflates them.

b. **Exhalation.** The rib cage movements and pressure relationships are reversed for exhalation. Thus, intrathoracic volume decreases. The intrathoracic pressure increases and forces air outside the body.

1-8. DIAPHRAGMATIC (ABDOMINAL) BREATHING

The diaphragm is a thin, but strong, dome-shaped muscular membrane that separates the abdominal and thoracic cavities. The abdominal wall is elastic in nature. The abdominal cavity is filled with soft, watery tissues.

a. **Inhalation**. As the diaphragm contracts, the dome flattens and the diaphragm descends. This increases the depth (vertical diameter) of the thoracic cavity and thus increases its volume. This decreases air pressure within the thoracic cavity. The greater air pressure outside the body then forces air into the lungs.

b. **Exhalation**. As the diaphragm relaxes, the elastic abdominal wall forces the diaphragm back up by pushing the watery tissues of the abdomen against the underside of the relaxed diaphragm. The dome extends upward. The process of inhalation is thus reversed.

Section III. CONDITIONS AFFECTING THE RESPIRATORY SYSTEM

1-9. INTRODUCTION

Many conditions affect the respiratory system. Some of the conditions are life-threatening, while many are chronic conditions which affect thousands of patients. Many of the patients who suffer from these conditions will be standing in front of the outpatient pharmacy in order to receive prescriptions to obtain some relief.

1-10. PNEUMONIA

Pneumonia is caused by an infection of the lung. This infection is caused by either bacteria (like the pneumococcus bacterium) or viruses. In pneumonia the walls of the alveoli become inflamed and filled with fluid and the air spaces in the alveoli become filled with blood and fluid. As you might expect, the exchange of gases in the alveoli becomes impaired. Death can result from pneumonia.

1-11. ASTHMA

Asthma, a condition usually caused by allergic reactions to substances in the environment, affects many people. The allergic reactions cause the bronchioles to spasm. Hence, the flow of air into and out of the lungs becomes impaired. For some unknown reason, the flow of air out of the lungs is more impeded than the flow of air into the lungs. Hence, the person with asthma often finds it more difficult to expire (expel the air) than to inspire. Furthermore, such labored breathing, after many years, often results in the asthma-sufferer having a barrel-shaped chest.

1-12. STATUS ASTHMATICUS

Status asthmaticus is a very sudden, continuous, and intense asthmatic attack.

1-13. EMPHYSEMA

Emphysema is a condition in which the patient has large portions of the alveolar walls destroyed. Consequently, the patient finds it necessary to breathe faster and more deeply in order to obtain the oxygen needed to live. Emphysema is often associated with smoking. Emphysema may also be referred to as chronic obstructive pulmonary disease (COPD).

1-14. PULMONARY EDEMA

Pulmonary edema is a condition in which fluid collects in the interstitial spaces of the lungs and in the alveoli. Obviously, the exchange of gases in the alveoli becomes impaired. Pulmonary edema is usually caused when the left side of the heart fails to pump efficiently. When this happens, blood backs up into the pulmonary circulation and causes fluid in the lungs.

Section IV. RESPIRATORY SYSTEM DRUGS

1-15. INTRODUCTION

Drugs affecting the respiratory system have been in use for years. In the first part of this century, for example, various members of the morphine family (that is, heroin) were used in the treatment of coughs. In the 1980s, people are using both legend and over-the-counter cough preparations. At certain times of the year you will see many prescriptions for cough medicines and expectorants. You have probably seen such increases when winter arrives. This section of the subcourse will discuss some respiratory systems medications commonly seen in the pharmacy.

1-16. ANTITUSSIVE AGENTS

a. **Background**. Antitussives are agents that relieve or prevent coughing. These agents, in general, act on the central nervous system to depress the cough reflex center in the medulla of the brain. Antitussives are used to reduce respiratory irritation. Such reduction of respiratory irritation results in the patient's being able to rest better at night because he is not kept awake by his coughing.

b. **Antitussive Agents**.

(1) Codeine. Codeine is considered to be the most useful narcotic antitussive agent. Codeine aids in relieving the pain (that is, producing analgesia) associated with a hacking cough. The main side effects associated with codeine include drowsiness, nausea, vomiting, and constipation. When a preparation containing codeine is dispensed to a patient that patient should be told that the product may cause drowsiness, and that he should not drink alcohol while taking the medication. Codeine is a Note R drug alone and cannot be refilled. It is a Note Q item when it is found in combination products (for example: Robitussin A-C Syrup). The usual oral dosage of codeine alone is 15 milligrams (1/4 grain) every 4 to 6 hours as needed for cough. The dosage can be increased but should not exceed 120 milligrams in 24 hours because of its central nervous system (CNS) depressant effects.

(2) Benzonatate (Tessalon®). Benzonatate is a nonnarcotic antitussive that produces its effect through a CNS depressant effect similar to codeine. Furthermore, it produces a local anesthetic effect on the stretch receptors in the lower respiratory tract, which control coughing. Benzonatate is usually given in 100 milligram doses--three to six times daily. This drug has few side effects except that it will numb the mouth, tongue, and pharynx if the capsules are chewed (this is because of its topical anesthetic effect). Benzonatate is available in the form of 100 milligram capsules.

(3) Dextromethorphan, DM (Pertussin CS®). Dextromethorphan is another nonnarcotic antitussive. It is found alone or in combination--usually with expectorants. The most common side effect associated with this drug is gastrointestinal (G.I.) upset. Dextromethorphan is a non-legend drug, which may be written as a prescription drug or as a hand-out item depending on the local policy of your hospital. The usual oral dosage of this drug is 10 to 30 milligrams, every four to eight hours. Do not exceed 120mg in 24 hours. There are many products on the market, which contain dextromethorphan in combination. Examples of such products include Robitussin-DM® and Baytussin-DM®.

1-17. EXPECTORANT AGENTS

a. **Background**. Expectorants are agents that facilitate the removal of secretions of the bronchopulmonary mucous membrane. Most of the expectorants discussed below act reflexively by irritating the gastric mucosa. This, in turn, stimulates secretions in the respiratory tract. Expectorants are used to remove bronchial secretions which are purulent (containing pus), viscid (thick), or excessive. The loosened material is then moved toward the pharynx through ciliary motion and coughing.

b. **Expectorant Agents**.

(1) Guaifenesin (Robitussin®, Baytussin®). Guaifenesin is the most commonly used expectorant today. This nonlegend drug has the side effect of gastrointestinal (G.I.) upset. Guaifenesin may be found alone as a syrup (100 milligrams per 5 milliliters), tablet 600 mg (Humibid® L.A.), or in many combination products such as Robitussin-DM®.

(2) Saturated Solution of Potassium Iodide. Saturated solution of potassium iodide (SSKI) is an expectorant administered as 300 milligrams (10 drops) in a glass of water or fruit juice every three or four times daily. SSKI has a very unpleasant taste. Overdoses of this product may lead to a condition known as iodism that produces an acne-type rash, fever, and rhinitis or runny nose. Patient compliance with this product may be low because of its unpleasant taste. Consequently, when the medication is dispensed you should tell the patient to place the required amount of SSKI in fruit juice in order to mask its taste. This drug is available in a saturated solution of 1 gram per milliliter in 30 milliliter containers.

(3) Elixir of Terpin Hydrate. Elixir of terpin hydrate (ETH) is an expectorant, which works directly on the bronchial secretory cells in the lower respiratory tract to facilitate the removal of bronchial secretions. It is usually given in doses, which range from 85 to 170 milligrams (1 or 2 teaspoonsful) 3 or 4 times daily. The side effects of this drug are related to its alcohol content (42 percent or 84 proof). If enough ETH is consumed it will produce significant CNS depression. Even with the high alcohol content, ETH is an Over the Counter (OTC) product. It is available as a syrup (85 milligrams per 5 milliliters) in 120 milliliter containers.

NOTE: Terpin Hydrate is no longer approved for use as an expectorant. It is used mainly as a vehicle for cough mixtures.

1-18. ANTITUSSIVE-EXPECTORANT COMBINATION PRODUCTS

The antitussive-expectorant combinations are used for a hyperactive nonproductive cough. The side effects of these drugs, or course, will be dependent on the antitussive-expectorant combination used. Some typical combination products used by the military are Robitussin-DM®, Robitussin® A-C Syrup, and Novahistine® Expectorant Liquid.

1-19. MUCOLYTICS

a. **Background.** Mucolytics are respiratory drugs that dissolve mucous in the respiratory tract. They are used by inhalation in an attempt to reduce the viscosity (thickness) of respiratory tract fluid. The loosened material can then be moved toward the pharynx more easily by ciliary motion and coughing. Like the expectorants, the mucolytics are used in the treatment of respiratory disorders in which the secretions are purulent (contain pus), viscid, or excessive. Consequently, the mucolytics represent an alternative to the oral use of expectorants.

b. **Mucolytic Agents**.

(1) Acetylcysteine (Mucomyst®). This is a mucolytic given by inhalation or nebulization. Nebulization is treatment by spray. Two to twenty milliliters of a 10 percent drug solution or 1 to 10 milliliters of a 20 percent Mucomyst® solution is nebulized into a face mask or mouth piece every two to six hours daily. Acetylcysteine has an unpleasant (like rotten eggs) smell. Side effects associated with this agent include nausea and vomiting and bronchospasms with higher concentrations (with the 20 percent solution). This medication is only dispensed for inpatient use--usually to the respiratory therapy clinic or to the nursing station. The sterile solution should be covered, refrigerated, and used within 96 hours after the vial is opened. It is available in 10 percent and 20 percent solutions in containers of 4, 10, or 30 milliliters.

(2) Sodium Chloride Solution U.S.P. (0.9 percent sodium chloride solution). This agent is used alone or in combination with other mucolytic agents. Sodium chloride solution increases the respiratory fluid volume by osmosis, which tends to decrease the viscosity of the respiratory fluid. It is also administered by inhalation in a nebulized form as a dense mist in a tent or delivered through a face mask or mouth piece. The main side effect seen with sodium chloride solution occurs after prolonged inhalation. This will cause localized irritation of the bronchial mucosa. Sodium chloride solution for this purpose is for inpatient use by respiratory therapy personnel or by nursing personnel. Concentrated Sodium Chloride (23.4%) is used by respiratory therapy to induce sputum production (sputum induction procedure).

1-20. BRONCHODILATOR AGENTS

a. **Background**. The bronchodilators are agents that cause expansion of the air passages of the lungs. This allows the patient to breathe more easily. Bronchodilators are of value in overcoming acute bronchospasms. They are employed as adjuncts in prophylactic and symptomatic treatment of the individual complications of obstructive pulmonary diseases such as asthma, bronchitis, and emphysema. Most of these agents have been discussed in other lessons of the pharmacology series.

b. **Bronchodilator Agents (Sympathomimetics).** Sympathomimetic bronchodilators act by relaxing contractions of the smooth muscle of the bronchioles. These agents are often referred to as “beta agonists”.

(1) Albuterol (Proventil, Ventolin). Albuterol is a short acting beta-agonist or bronchodilator. It is used in the relief and prevention of bronchospasm and in the prevention of exercise-induced bronchospasm. Albuterol is available as an inhalation aerosol, inhalation solution, inhalation capsules, regular and sustained release tablets, and syrup. Other than the sustained release products, it is prescribed every 4 to 6 hours. Albuterol is often used as “rescue therapy” due to its quick onset of action.

(2) Salmeterol (Serevent). Salmeterol is indicated for the same conditions as albuterol, however its distinct advantage is that it is administered twice daily. It is available as an inhalation aerosol. Salmeterol CANNOT be used for “rescue therapy”; a short acting beta agonist such as albuterol must be used.

(3) (Epinephrine (Adrenalin). Epinephrine is used as a bronchodilator because of its beta effects on the bronchi and a pharmacologic antagonist of histamine. Epinephrine is employed for the treatment of acute attacks of bronchospasms associated with emphysema, bronchitis, or anaphylaxis. The inhalation route is not the preferred route of administration; however, it may be used. Epinephrine is usually administered subcutaneously when used and is fairly effective at reducing bronchospasms.

(4) Metaproterenol (Alupent®, Metaprel®). This is an adrenergic agent that has primary beta2 activity. That is, its main effect is to relax the bronchioles. It has the same indications as epinephrine. It may be used for the prevention of bronchospasms associated with chronic obstructive pulmonary diseases. Inhalation of metaproterenol may be used in the treatment of mild bronchospasm attacks. Metaproterenol is somewhat more effective than inhaled isoproterenol. Metaproterenol's duration of action is substantially longer than that of isoproterenol.

(5) Ephedrine. Ephedrine has actions of those similar to those of epinephrine. Ephedrine is not frequently used because of the availability of other more suitable agents. Ephedrine is administered orally. It is used to treat mild bronchospasm attacks and prophylactically to prevent bronchospasm attacks. Ephedrine is not as suitable as epineprhine for the treatment of severe attacks of bronchial asthma because its bronchodilator action is weaker.

(6) Isoproterenol (Isuprel®). Isoproterenol is an adrenergic agent used to treat asthma, bronchitis, and emphysema. Like metaproterenol, isoproterenol is administered by inhalation for the treatment of mild bronchospasms. Isoproterenol may be administered intravenously with great caution to treat status asthmaticus.

(7) Other sympathomimetic bronchodilators include Terbutaline (Brethine), Pirbuterol (Maxair), and Bitolterol mesylate (Tornalate).

c. **Bronchodilator Agents (Xanthine derivatives).** The methylxanthines (theophylline and derivatives) directly relax the smooth muscle of the bronchi and pulmonary blood vessels. They may also reduce the fatigability and thereby improve contractility in patients with chronic obstructive airway disease. Xanthine derivatives are often used in the treatment of apnea and bradycardia of prematurity in infants.

(1) Aminophylline. Aminophylline is a xanthine derivative containing ~80% theophylline. It is prescribed as a bronchodilator to treat asthma. It will also relieve bronchospasms associated with emphysema and bronchitis. Aminophylline may be administered orally or rectally to prevent severe attacks of bronchial asthma but is generally administered intravenously (I.V) to relieve acute bronchospasm or status asthmaticus resistant to adrenergic drugs.

(2) Theophylline (Theolair, Slo-Phyllin, Theodur). Theophylline is often prescribed as the xanthine of choice for oral administration (tablets, capsules, elixir, syrup, or solution). One must take care when dispensing theophylline products. Each different brand varies in the actual amount of theophylline contained in the product and in the duration of action. Theophylline is a drug with a very narrow therapeutic index (the treatment dose is very close to the toxic dose). For this reason, patients should have their theophylline blood levels monitored on a routine basis.

d. **Miscellaneous Respiratory Agents.**

(1) Cromolyn (Intal®). Cromolyn is a unique product that works by inhibiting the release of histamine and other spasm-causing compounds from mast cells located in the lungs and prevents bronchoconstriction. It is used mainly for the treatment or prevention of mild bronchospasms associated with asthma. It is available as an inhalation aerosol and nebulization solution.

(2) Leukotriene modifiers. The production of leukotrienes (immunologic proteins) and the binding of leukotriene receptors appears to be responsible for airway edema, smooth muscle constriction and altered inflammatory processes contributing to the signs and symptoms of asthma. For this reason, several new agents have been developed.

(a) Zafirlukast (Accolate®), Montelukast (Singulair®). Both of these agents are leukotriene receptor antagonists which cause inhibition of bronchoconstriction. Zafirlukast is available as a tablet prescribed twice daily. Montelukast is prescribed as a once daily tablet.

(b) Ziluton (Zyflo®), Ziluton works a little differently in that it inhibits the formation of leukotrienes to prevent bronchoconstriction. Ziluton is administered four times daily.

Continue with Exercises

EXERCISES, LESSON 1

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. External respiration is:

   a. The exchange of gases between the atmosphere and the cells of the body.

   b. The exchange of gases between the blood and the individual cells of the body.

   c. The exchange of gases between the air in the lungs and blood.

   d. The aeration of the lungs.

2. Bronchi are:

   a. Tubes that lead from the larynx to the lungs.

   b. Tubes that warm and humidify the air as it enters the lungs.

   c. Tubes that extend into the nasal chamber in order to increase the surface area exposed to inflowing air.

   d. Tubes that lead from the trachea to the lungs.

3. Which of the following statements best describes the paranasal sinuses?

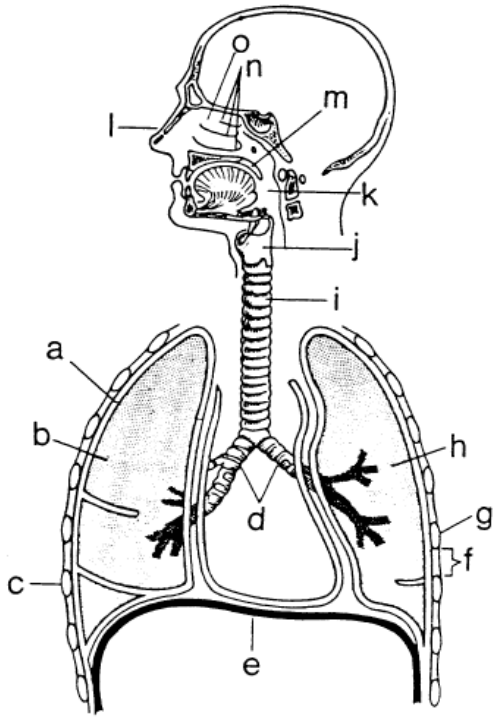
   a. Air cells or cavities in the skull that are connected with the nasal chambers and lined with ciliated mucoperiosteum.

   b. Special nerve endings located in the upper areas of the nasal chambers.

   c. The portion of the pharynx that is common to both the respiratory and digestive systems.

   d. The vestibules that are covered by the epiglottis.

REFER TO THE FIGURE BELOW AS YOU ANSWER QUESTIONS 4 AND 5.



The human respiratory system.

4. Which letter in the illustration above refers to the bronchi?

   a. a

   b. b

   c. c

   d. d

5. Which letter in the illustration above refers to the pleural space?

   a. a

   b. b

   c. c

   d. d

6. Which of the statements below best describes abdominal breathing?

    a. Breathing which occurs because of the contractions of the small intestine and other abdominal organs.

    b. Breathing which occurs because of changes in the intrathoracic volume.

    c. Breathing which occurs because of the contraction and relaxation of the diaphragm.

    d. Breathing which occurs because of changes in the position of the rib cage.

7. Pneumonia is best described as:

    a. A condition in which fluid collects in the interstitial spaces of the lungs caused by the left heart's inability to pump efficiently.

    b. An infection of the lungs caused by bacteria or viruses in which the walls of the alveoli become inflamed.

    c. A condition in which the patient has large portions of the walls of the alveoli destroyed.

    d. A state of impaired breathing caused by spasms of the bronchi.

8. Mucolytic agents are drugs that:

    a. Relieve bronchospasms.

    b. Dissolve mucous in the respiratory tract.

    c. Are used to irritate the gastric mucosa.

    d. Relieve or prevent coughing.

9. Acetylcysteine is used as a(n):

   a. Antitussive agent.

   b. Mucolytic agent.

   c. Expectorant agent.

   d. Bronchodilator.

10. Elixir of Terpin Hydrate is used as a(n):

   a. Expectorant.

   b. Antitussive.

   c. Mucolytic.

   d. Bronchodilator.

11. Match the drug name in Column A with its trade name in Column B.

Column A	Column B
_____Acetylcysteine.	a. Isuprel®.
_____Metaproterenol.	b. Alupent®.
_____Guaifenesin.	c. Tessalon®
_____Cromolyn.	d. Mucomyst®.
_____Isoproterenol.	e. Intal®.
_____Benzonatate.	f. Baytussin®.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 1

1. c (para 1-1a)
2. d (para 1-5a)
3. a (para 1-3b(4))
4. d (figure 1-1)
5. a (figure 1-1)
6. c (para 1-8)
7. b (para 1-10)
8. b (para 1-19a)
9. b (para 1-19b(1))
10. a (para 1-17b(3))

11.

COLUMN A		COLUMN B
__d__ Acetylcysteine. (para 1-19b(1))	a.	Isuprel®.
__b__ Metaproterenol. (para 1-20b(2))	b.	Alupent®.
__f__ Guaifenesin. (para 1-17b(1))	c.	Tessalon®.
__e__ Cromolyn. (para 1-20b(6))	d.	Mucomyst®.
__a__ Isoproterenol. (para 1-20b(4))	e.	Intal®.
__c__ Benzonatate. (para 1-16b(2))	f.	Baytussin®.

End of Lesson 1

LESSON ASSIGNMENT

SUBCOURSE MD0806 Therapeutics III.

LESSON 2 The Human Cardiovascular and Lymphatic Systems.

LESSON ASSIGNMENT Paragraphs 2-1--2-22.

LESSON OBJECTIVES After you finish this lesson you should be able to:

2-1. Given a group of statements, select the statement that best explains the need for circulatory systems.

2-2. Given a group of systems, select the two circulatory systems in the human body.

2-3. Given the name of one of the major components of the human circulatory system and a group of statements, select the statement that best describes that component.

2-4. Given a group of components, select the components of blood.

2-5. From a group of statements, select the statement that best describes either the plasma or the formed elements of the blood.

2-6. Given a group of statements and the names of one of the formed elements of the blood, select the statement that best describes the given formed elements.

2-7. From a group of functions, select the function(s) of the blood.

2-8. Given a group of statements and one of the types of blood vessels, select the statement that best describes that type of blood vessel.

2-9. Given the steps of blood clotting in an unsequential order and several selections of varying sequence, select the sequence of blood clotting as the steps actually occur.

2-10. From a group of statements, select the definition of the term blood pressure, systolic blood pressure, and diastolic blood pressure.

2-11. Given a group of medical problems and one of the following conditions: hypertension and hypotension, select the medical problem(s) associated the given condition.

2-12. Given a group of statements and the name of a disorder affecting the circulatory system, select the statement that best describes the disorder.

2-13. Given a drawing of either the anterior or the interior view of the human heart and a list of names of parts of the heart, match the name of each part of the heart with its location.

2-14. From a group of statements, select the statement that best describes the property of inherent rhythmicity.

2-15. Given one of the following: sinoatrial node, atrioventricular node, bundle of His, or Purkinje fibers and a group of statements; select the statement that best describes the role of the given heart structure in the heartbeat.

2-16. Given one of the following electrolytes: sodium, potassium, or calcium and a group of statements, select the statement which best describes the effect(s) of abnormal amounts of that electrolyte on the myocardium.

2-17. Given the name of a cardiac disorder and a group of statements, select the statement that best describes that disorder.

2-18. Given the name of one of the structures of the human lymphatic system and a group of statements, select the statement that best describes that structure.

SUGGESTION

After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 2

THE HUMAN CARDIOVASCULAR AND LYMPHATIC SYSTEMS

Section I. INTRODUCTION

2-1. NEED FOR CIRCULATORY SYSTEMS

a. The need for circulatory systems is based on two criteria:

(1) Number of cells. Multicellular animals are animals with great numbers of cells.

(2) Size. In larger animals, most cells are too far away from sources of food and oxygen for simple diffusion to provide sufficient amounts. Also, distances are too great for simple removal of wastes.

b. Because of these criteria, we need a system (or systems) to carry materials to all cells. To get food and oxygen to the cells and to remove waste products, we need a transport system, or circulatory system. Human circulatory systems are so effective that few cells are more than the width of two cells away from a capillary.

2-2. BASIC COMPONENTS OF ANY CIRCULATORY SYSTEM

The four basic components of any circulatory system are a vehicle, conduits, a motive force, and exchange areas.

a. **Vehicle.** The vehicle is the substance that actually carries the materials being transported.

b. **Conduits**. A conduit is a channel, pipe, or tube through which a vehicle travels.

c. **Motive Force**. If we say that a force is motive, we mean that it produces movement. Systems providing a motive force are often known as pumps.

d. **Exchange Areas**. Since the materials being transported must eventually be exchanged with a part of the body, special areas are developed for this purpose. They are called exchange areas.

2-3. CIRCULATORY SYSTEMS IN THE HUMAN BODY

a. The cardiovascular system is the circulatory system involving the heart and blood vessels.

b. The lymphatic system is a drainage-type circulatory system involved with the clear fluid known as lymph.

c. There are other minor circulatory systems in the human body, such as the one involved with cerebrospinal fluid.

Section II. THE HUMAN CARDIOVASCULAR SYSTEM

2-4. GENERAL

The human cardiovascular system is a collection of interacting structures designed to supply oxygen and nutrients to living cells and to remove carbon dioxide and other wastes. Its major components are the:

a. **Blood**. Blood is the vehicle for oxygen, nutrients, and wastes.

b. **Blood Vessels**. Blood vessels are the conduits, or channels, through which the blood is moved.

c. **Heart**. The heart is the pump that provides the primary motive force.

d. **Capillaries**. The capillaries, minute (very small) vessels, provide exchange areas. For example, in the capillaries of the lungs, oxygen is added and carbon dioxide is removed from the blood.

2-5. BLOOD

Blood is the vehicle for the human cardiovascular system. Its major subdivisions are the plasma, a fluid containing proteins, and the formed elements, which includes red blood cells, white blood cells, and platelets.

a. **Plasma.**

(1) Plasma makes up about 55 percent of the total blood volume. It is mainly composed of water. A variety of materials are dissolved in plasma. Among the most important of these are proteins.

(2) After the blood clots, the clear fluid remaining is called serum. Serum does not contain the proteins used for clotting. Otherwise, it is very similar to plasma.

b. **Formed Elements**. The formed elements make up about 45 percent of the total blood volume. The formed elements are cellular in nature. While the red blood cells (RBCs) and white blood cells (WBCs) are cells, the platelets are only fragments of cells.

(1) Red blood cells (erythrocytes). Red blood cells (RBCs) are biconcave discs. That is, they are shaped something like an inner tube from an automobile tire, but with a thin middle portion instead of a hole. There are approximately 5,000,000 RBCs in a cubic millimeter of normal adult blood. Red blood cells contain hemoglobin, a protein that carries most of the oxygen transported by the blood.

(2) White blood cells (leukocytes). There are various types of WBCs, but the most common are neutrophils and lymphocytes. Neutrophils phagocytize (swallow up) foreign particles and organisms, and digest them. Lymphocytes produce antibodies and serve other functions in immunity. In normal adults, there are about 5,000 to 11,000 WBCs per cubic millimeter of blood.

(3) Platelets. Platelets are about half the size of erythrocytes. They are fragments of cells. Since they are fragile, they last only about 3-5 days. Their main function is to aid in clotting by clumping together and by releasing chemical factors relating to clotting. There are 150,000-350,000 platelets in a cubic millimeter of normal blood.

c. **Some General Functions of the Blood**.

(1) Blood serves as a vehicle for oxygen, nutrients, carbon dioxide and other wastes, hormones, antibodies, heat, and so forth.

(2) Blood aids in temperature control. Beneath the skin, there is a network of vessels that functions much like a radiator. To avoid accumulation of excess heat in the body, the flow of blood to these vessels can be increased greatly. Here, aided by the evaporative cooling provided by the sweat glands, large amounts of heat can be rapidly given off. The flow of blood also keeps the outer parts of the body from becoming too cold.

(3) The blood aids in protecting our bodies by providing immunity. Some WBCs phagocytize (swallow up) foreign particles and microorganisms. Other WBCs produce antibodies. The blood transports antibodies throughout the body.

(4) Blood clotting is another function of blood. Not only does this prevent continued blood loss; it also helps prevent invasion of the body by microorganisms and viruses by sealing the wound opening.

2-6. BLOOD VESSELS

The blood is conducted or carried through the body by tubular structures known as blood vessels. Since at no time does the whole blood ever leave a blood vessel of some sort, we refer to this system as a closed system.

a. **General Construction**. The blood vessels in general are tubular and have a three-layered wall.

(1) Intima. A layer of smooth epithelium known as the intima lines the lumen (hollow central cavity).

(2) Media. A middle layer of smooth muscle tissue is called the media.

(3) Adventitia. The adventitia is the outer layer of fibrous connective tissue that holds everything together.

b. **Types of Blood Vessels**. See figure 2-1 for a diagram of the human circulatory system. We recognize three types of blood vessels:

(1) The arteries carry blood away from the chambers of the heart.

(2) The veins carry blood to the chambers of the heart.

(3) Capillaries are extremely thin-walled vessels having only the intimal layer through which exchanges can take place between the blood and the tissue cells.

c. **Relationships.** Arteries and veins are largest where they are closest to the heart. Away from the heart, they branch into smaller and smaller and more numerous vessels. The branching continues until the smallest arteries (arterioles) empty into the capillaries. The capillaries in turn are drained by the venules of the venous system.

d. **Valves**. Within the heart and the veins are structures known as valves. Valves function to insure that the blood flows in only one direction.

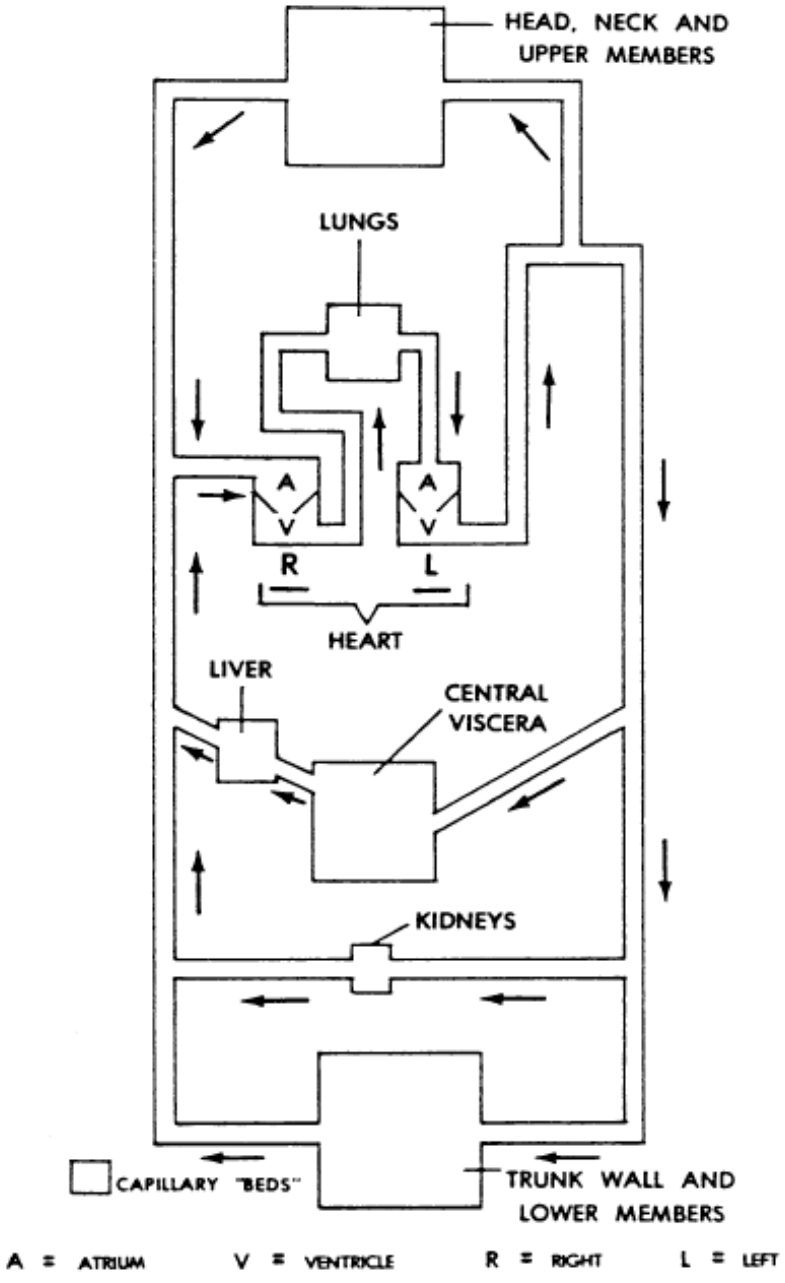


Figure 2-1. Diagram of the human circulatory system.

2-7. BLOOD CLOTTING

Blood clotting is a process that is dependent on several different factors. This process is also known as hemostasis. There are three general mechanisms involved in blood clotting: vascular spasm, the platelet plug, and the clotting mechanism.

a. **Vascular Spasm**. When a blood vessel is cut, the vascular spasm causes rapid constriction of the cut blood vessel. This decreases the amount of blood lost. The mechanism by which this mechanism occurs is not fully known, but it appears to be a reflex response initiated by pain. It is interesting to note that when a vessel is cut by crushing, the vascular spasm response seems to occur more rapidly and more intensely than if the vessel is quickly cut (as with a knife). After the vascular spasm has occurred, the second mechanism involved with the clotting process--the platelet plug--occurs.

b. **Platelet Plug**. The blood platelets circulate freely in the blood until they reach a blood vessel that has been severed. Platelets then adhere to the ruptured point of the blood vessel. After a period of time, the platelets partially plug the severed vessel.

c. **Clotting Mechanism**. The third mechanism involves the formation of the blood clot. The clot forms within three to six minutes after the rupturing of the blood vessel. In about 30 minutes the clot shrinks; thus pulling the end of the severed vessel in to close the diameter of the vessel even further.

2-8. MECHANISMS OF BLOOD CLOTTING

The actual clotting mechanisms involve several steps (see table 2-1). Each step is essential to clotting.

STEP 1:	The blood platelets release a substance that is known as thromboplastin.
STEP 2:	Thromboplastin reacts with calcium and another substance, prothrombin, to form thrombin. Vitamin K is necessary for the proper formation of prothrombin.
STEP 3:	The thrombin formed acts as an enzyme to convert fibrinogen to fibrin threads that eventually form the blood clot.

Table 2-1. Steps in blood clotting.

NOTE: For a more in-depth discussion of blood clotting you should locate and read a physiology text that is appropriate to your level of understanding.

2-9. BLOOD PRESSURE

a. **Introduction**. Blood pressure is the force exerted by the blood as it is pumped throughout the circulatory system. Blood pressure is needed by the body for the perfusion and distribution of nutrients throughout the body. Blood pressure is expressed in numerical values with the use of an instrument such as the sphygmomanometer. Blood pressure is expressed as systolic blood pressure over diastolic blood pressure (for example, 120/70). Systolic blood pressure is the pressure of blood as it is being pumped from the heart. When the heart contracts, it is said to be in systole. Diastolic pressure is the residual pressure of the blood because of the elasticity of the blood vessels (when the heart is at rest).

b. **Regulation**. In order to regulate blood pressure to meet the immediate needs of the body, the body is equipped with various systems that can change the blood pressure both by a change in the size of the openings of the various blood vessels and by a change in the volume of the blood (that is, blood plasma).

(1) Baroreceptors. Baroreceptors are located in the aortic arch of the aorta and in the internal carotid arteries. Baroreceptors are really a series of specialized neurons that function as rapidly acting blood pressure regulators. They sense changes in blood pressure and act in a reflex manner to change both the rate and force of the contraction of the heart and the size of the openings of the blood vessels.

(2) Chemoreceptors. Chemoreceptors are receptors which sense changes in the oxygen content of the blood. They are located in high numbers in the aortic arch and internal carotid arteries. The chemoreceptors have a dual purpose in that they help to regulate blood pressure in addition to the regulation of blood pressure. The change in blood pressure they produce is due mainly to the change in heart rate. Working in conjunction with the chemoreceptors is a mechanism known as the CNS ischemic response. The CNS ischemic response senses an increase in carbon dioxide and lactic acid (both waste products of metabolism) in the blood and reacts to increase or decrease heart rate to maintain these products within normal amounts. The CNS ischemic response generally decreases the heart rate so that blood spends a longer time in the lungs thereby allowing for an increased exchange of oxygen and carbon dioxide.

c. **Correction of Blood Pressure**. Blood pressure is corrected by changing blood vessel tone and cardiac output. The baroreceptors eventually adapt to whatever pressure level to which they are exposed. Therefore, prolonged regulation of arterial pressure requires other control systems. Kidney malfunctions, fluid shifts, and electrolyte imbalances will eventually occur if this condition is not corrected. These are also known as long term regulators.

d. **Renal Fluid-Volume Mechanism.** The renal fluid-volume mechanism is one of the long-term regulators located in the kidneys. This mechanism works by causing changes in the amount of water reabsorbed by the kidneys. An increase in water reabsorption leads to an increase in blood pressure and a decrease in water reabsorption leads to a corresponding decrease in the blood pressure. The secretion of certain hormones also affects blood pressure. Aldosterone, a hormone secreted by the adrenal cortex, leads to an increase in sodium retention. This increase in sodium retention leads to a corresponding increase in water retention with an overall effect of higher blood pressure.

2-10. ABNORMAL BLOOD PRESSURE

a. **Hypertension.** Hypertension is characterized by a persistent increase in blood pressure. It should be noted that there are always periodic increases in blood pressure due to times of stress or physical exertion. However, if the blood pressure remains at these high levels serious complications could result. Some of the effects of hypertension on the body are frequent nosebleeds, strokes, hypertrophy of the myocardium, and arteriosclerosis. Hypertension is one of the easiest disorders to treat if it is detected early. Drug therapy consists of diuretics and other antihypertensives. It is essential for the patient who has controlled his blood pressure by the use of medication to continue to take that medication even after the outward signs and symptoms subside.

b. **Hypotension**. Hypotension is defined as persistent and abnormal low blood pressure. This condition is not usually fatal in itself; however, the hypotensive patient is much more susceptible to shock in case of a rapid loss of blood. Many times low blood pressure is observed in persons who exercise a great deal. When hypotension becomes serious, it can be treated by drug therapy. Effects of hypotension on the body include general fatigue and weakness and decreased kidney function. An increase in the susceptibility to orthostatic hypotension (that is, the patient faints when arising too quickly from a bed or chair) or fainting is also seen.

2-11. DISORDERS WHICH AFFECT THE BLOOD SYSTEM

As with any other system of the body, some disorders may affect the blood system. Usually these disorders are types of anemias, but there are other disorders involved.

a. **Iron Deficiency Anemia**. Iron deficiency anemia is due to a deficiency of elemental iron in the blood. Iron is essential for the proper functioning of hemoglobin. In iron deficiency anemia, the blood cannot transport as much oxygen. Therefore, the tissues of the body are deprived of the much-needed oxygen. Furthermore, the presence of iron deficiency anemia affects the formulation of blood cells. Treatment of iron deficiency anemia requires the administration of iron either orally or parenterally.

b. **Hemolytic Anemia**. Hemolytic anemia is a general term referring to anemias caused by weakened red blood cell membranes. There are several types of hemolytic anemias that are often classified according to their cause. Some of the causes of hemolytic anemia are drugs (such as primaquine or the sulfonamides), heredity, or lack of either vitamin B_{12} or folic acid. In hemolytic anemia, the red blood cells are weak and lyse (break apart) as they squeeze through the small capillaries or spleen. The treatment of the hemolytic anemias is obviously dependent on the particular cause. Splenectomies, discontinuance of the causative agent, or the administration of folic acid or vitamin B_{12} are some of the treatment possibilities.

c. **Sickle Cell Anemia**. Sickle cell anemia is a serious anemia that is predominant in people of black race. The erythrocytes of a person who has sickle cell anemia become sickle-shaped and, therefore, are not efficient carriers of gases or nutrients. The sickle-shaped cells also increase the viscosity of the blood that leads to decreased circulation in the small arteries and capillaries. Symptoms of sickle-cell anemia include pain of certain organs, bone and joint pain, fever, and cerebral thrombosis. The spleen is not usually enlarged. Complications associated with sickle cell anemia are leg ulcers, osteomyelitis, and occasionally, cardiac enlargement. The treatment for sickle cell anemia is usually symptomatic as the actual cause of the condition is unknown. Blood transfusions are usually involved in most treatment regimens.

d. **Aplastic Anemia**. Aplastic anemia is a very serious and usually fatal condition that affects about four out of every one million people. It is characterized by a progressive degeneration of the bone marrow that is rarely reversible. The usual cause appears to be toxins or drugs and excessive use of X-rays. The prognosis of this severe bone marrow depression is generally poor.

e. **Hemophilia**. Hemophilia is usually a hereditary disease characterized by a lack of one of the factors necessary for the clotting of the blood. Hemophilia is a disease that occurs more commonly in men than women. Patients who have hemophilia do not usually develop massive hemorrhages, but rather slow oozing or trickling of blood. The primary danger with hemophiliac patients is trauma involving severe bleeding. In these cases, the patient may soon die because of a severe loss of blood that will occur if the missing clotting factor is not soon administered.

f. **Leukemia**. Leukemia is a disease of the white blood cell forming tissue. It is characterized by an abnormally high white blood cell count. During the progression of the disease, the white blood cells gradually crowd out the erythrocytes and in some cases the leukocytes phagocytize (engulf) the red blood cells.

g. **Mononucleosis**. Mononucleosis is an extremely contagious disease characterized by an abnormally large number of one type of white blood cells (the monocytes). The disease affects the lymph tissue and is characterized by fever, sore throat, and inflamed lymph nodes. The spleen may become enlarged and lassitude (general tired feeling) on the part of the patient is not uncommon. Mononucleosis is thought to be a disease of viral origin that usually strikes people between the ages of ten and thirty-five. The treatment of mononucleosis is symptomatic. The disease usually runs its complete course in about four to six weeks.

h. **Pernicious Anemia**. Pernicious anemia is caused by the inability of the body to absorb vitamin B12 from the intestine. This failure to absorb vitamin B_{12} is caused by a lack of the intrinsic factor that is normally secreted by the parietal cells in the stomach. The presence of this intrinsic factor is needed in order to absorb vitamin B_{12}. Perncious anemia rarely affects persons under the age of thirty-five. It is more common in persons of English, Scandinavian, and Irish descent. It may be difficult to detect this condition because there are few outwardly visible signs associated with it. As with all anemias, fatigability is usually the first noticeable symptom. The red blood cells are large and oval. The treatment of pernicious anemia centers on the parenteral administration of vitamin B_{12} (cyanocobalamin) which must be continued for the remainder of the patient's life.

2-12. DISORDERS ASSOCIATED WITH THE CIRCULATORY SYSTEM

Two rather acute disorders that affect the circulatory system are a thrombus and an embolus. They are not considered diseases, but acute disorders.

a. **Thrombus.** A thrombus is a clot formed in a blood vessel that remains attached to the wall of the vessel. A thrombus can conceivably occur in any blood vessel. However, they are of primary concern when they occur in vessels serving vital organ systems such as the liver, kidneys, brain, and heart. Thrombi frequently get larger within the vessel and, if untreated, may eventually lead to complete blockage of the vessel. Such a blockage could lead to an infarction, an area of necrosis in a tissue or organ resulting from the obstruction of circulation to that area.

b. **Embolus**. If the thrombus becomes dislodged from the wall of the vessel, it becomes an embolus. The usual treatment for an embolus is anticoagulant therapy in an effort to decrease the possibility of any future clotting. If necessary, certain enzymes may be administered to the patient in order to dissolve the existing clot. Treatment of an embolus is nearly impossible until it becomes an embolism. When the embolism has been identified, the treatment usually involves bed rest, anticoagulant therapy, and the possible administration of fibrinolytic enzymes.

2-13. VASCULAR DISORDERS

Vascular disorders comprise some of the most common disorders in humans. Usually symptoms of vascular disorders are not seen until the condition reaches a point where it is considered serious. Several vascular disorders are discussed below:

a. **Arteriosclerosis.** A loss of elasticity or hardening of the arterial walls characterizes arteriosclerosis. The result is a decrease in the ability of these arteries to change their diameter. A complication that usually accompanies arteriosclerosis is atherosclerosis. Atherosclerosis is a condition in which lipid (fat) deposits form on the inside of the arteries causing a decrease in the flow of blood through the arteries. Both these conditions show a higher incidence in diabetics and in overweight individuals. Surgery and antihyperlipidemic drugs are used to treat these conditions.

b. **Varicose Veins**. A varicose vein is a condition that is probably because of excessively prolonged pooling of blood in the lower extremities (for example: legs). Varicose veins are especially common in people who are required to stand for prolonged periods of time with little or no exercise.

c. **Peripheral Vascular Disease**. Peripheral vascular disease is characterized by vasoconstriction of the arteries (especially in the extremities). Decreased blood flow to the extremities and corresponding hypothermia are some of the usual signs of this condition.

2-14. BONE MARROW DEPRESSION

Bone marrow depression is a condition characterized by a decrease in the function of the bone marrow that leads to a reduction in the cellular components of the blood. The overall effect of bone marrow depression is anemia and susceptibility to infection. The most common cause of bone marrow depression seems to be the toxicity of drugs. If detected early, the reversal of the disease may be accomplished by the removal of the causative agent (for example, the drug).

Section III. THE HEART AND THE SYSTEMIC CIRCULATION OF BLOOD

2-15. THE HEART

Through the action of its very muscular walls, the heart produces the primary motive force to drive the blood through the arterial system. In humans, the heart is located just above the diaphragm, in the middle of the thorax, and extending slightly to the left. It is said that the heart of an average individual is about the size of that individual's clenched fist.

a. **General Construction of the Human Heart**. See figure 2-2 for an illustration of the human heart.

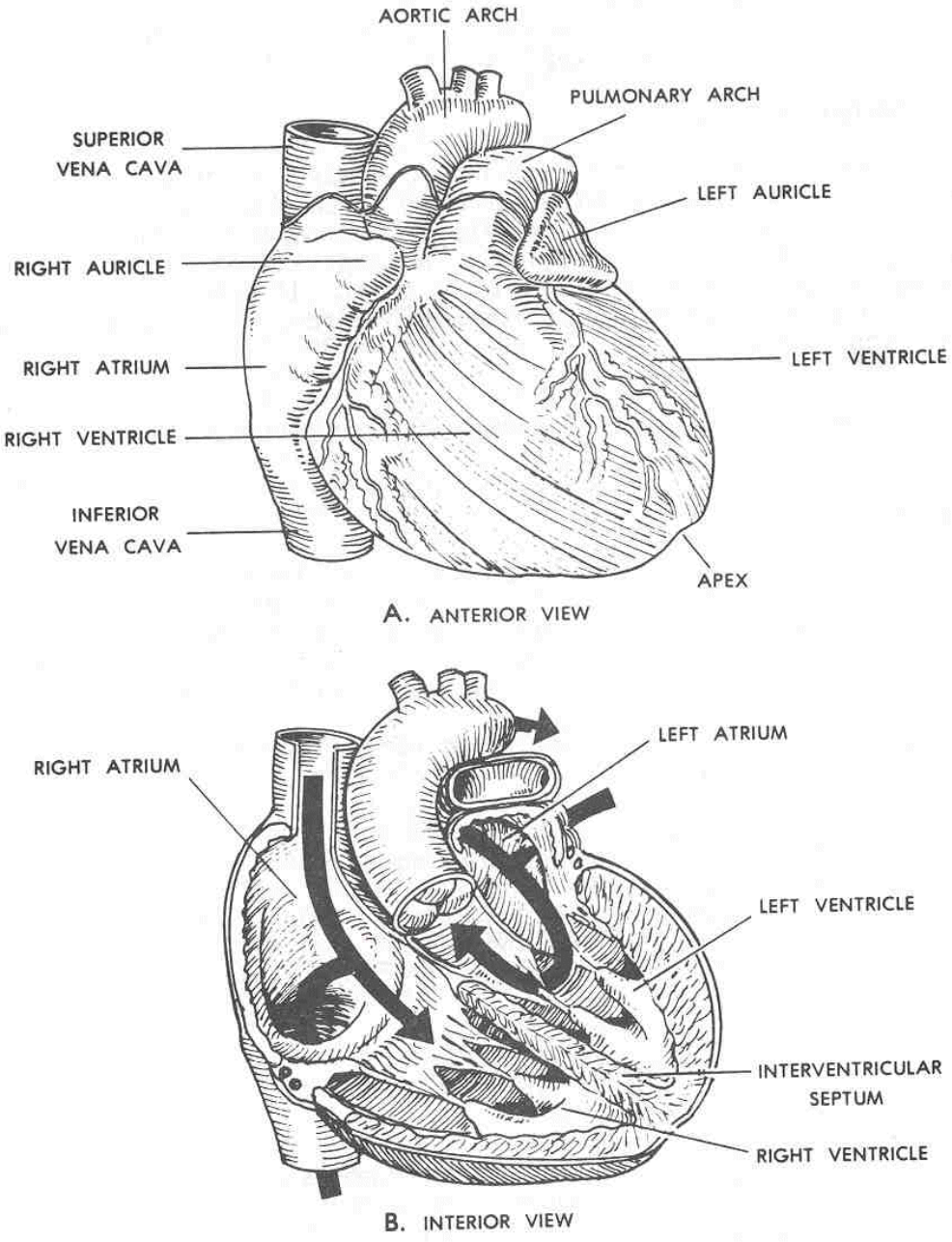


Figure 2-2. The human heart.

(1) Chambers. The heart is divided into four cavities known as the chambers. The upper two chambers are known as the atria, right and left. Each atrium has an ear-like projection known as an auricle. The lower two chambers are known as ventricles, right and left. Between the two atria is a common wall known as the interatrial septum. Between the two ventricles is a common wall known as the interventricular septum.

ATRIUM	=	hall
AURICLE	=	ear-like flap
VENTER	=	belly
SEPTUM	=	fence

(2) Wall layers. The walls of the chambers are in three general layers. Lining the cavity of each chamber is a smooth epithelium known as the endocardium. (Endocarditis is an inflammation of the endocardium.) The middle layer is made up of cardiac muscle tissue and is known as the myocardium. The outer layer of the heart is another epithelium known as the epicardium.

(3) Relationship of wall thickness to required pressure levels. A cross-section of the chambers shows that the atrial walls are relatively thin. The right ventricular wall is much thicker. The left ventricular wall is three to five times thicker than that of the right. These differences in wall thickness reflect the amount of muscle tissue needed to produce the amount of pressure required of each chamber.

(4) Cardiac valves. See figure 2-3.

(a) Between the atrium and ventricle of each side is the atrioventricular (A-V) valve. Each A-V valve prevents the blood from going back into the atrium from the ventricle of the same side. The right A-V valve is known as the tricuspid valve. The left A-V valve is known as the mitral valve. (“Might is never right.”). The mitral valve is sometimes called the bicuspid valve. The leaflets (flaps) of the A-V valves are prevented from being pushed back into the atria by fibrous cords. These fibrous cords are attached to the undersides (the ventricular side) of the leaflets and are called chordae tendineae. At their other ends, the chordae tendineae are attached to the inner walls of the ventricles by papillary muscles.

(b) A major artery leads away from each ventricle: the pulmonary trunk from the right ventricle and the aortic arch from the left ventricle. A semilunar valve is found at the base of each of the pulmonary trunk and the aortic arch. These semilunar valves prevent blood from flowing back into the ventricles. The pulmonary (semilunar) valve and the aortic (semilunar) valve are each made up of three semilunar (“pocket-like”) cusps.

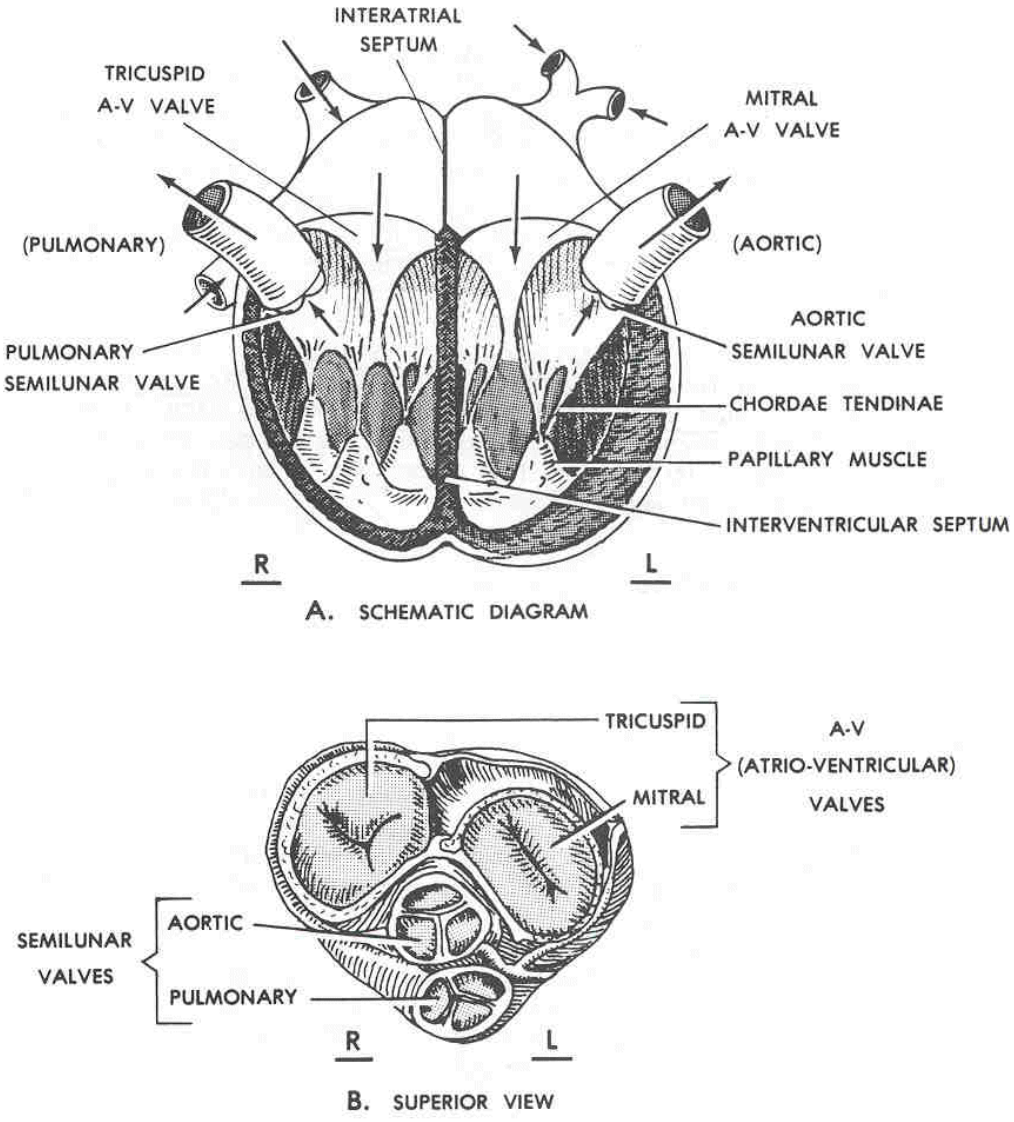


Figure 2-3. Scheme of heart valves.

b. **Coronary Arteries and Cardiac Veins.** We may say that the heart deals with two different kinds of blood flow: "functional" blood and "nutritive" blood. "Functional" blood is the blood that the heart works on, or pushes with its motive force. However, the walls of the heart require nutrition that they cannot get directly from the blood within the chambers. "Nutritive" blood is supplied to these walls by the coronary arteries, right and left. The coronary arteries arise from the base of the aortic arch and are distributed over the surface of the heart. This blood is collected by the cardiac veins and empties into the right atrium of the heart. Should a coronary artery, or one of its branches, become closed for whatever reason, that part of the heart wall formerly supplied nutrient blood by the closed vessel will very likely die.

c. **Pericardial Sac**. The average heart contracts in what is known as a heart beat, about 70-80 times a minute. To reduce the frictional forces that would be applied to its moving surfaces, the heart is enclosed in a special serous sac known as the pericardium ("around the heart").

2-16. THE PROPERTY OF INHERENT RHYTHMICITY

a. The heart muscle (myocardium), like other muscles, is dependent upon electrical energy for its proper contraction. One property of cardiac muscle that cannot be found in any other muscle is inherent rhythmicity. Inherent rhythmicity is the property of the cardiac muscle that allows cardiac muscle cells to beat separately without any stimulation. If a cardiac muscle cell is placed in a saline (salt) bath containing the required amount of essential electrolytes the muscle cell will contract and relax rhythmically with no external stimulation. Furthermore, if another cardiac cell is placed in the same bath, it, too, will beat at its own separate rate. It is interesting that when the two cardiac cells are placed together (in contact) the two cells will begin to beat as a unit. The property of inherent rhythmicity allows the myocardium to beat together with a minimal amount of nervous stimulation.

b. Instead of initiating the contractile process, nervous stimulation functions rather to govern the rate of the heartbeat. The property of inherent rhythmicity appears to be embryonic in origin. That is, the heart begins beating and systemic circulation occurs before any nervous tissue is formed.

2-17. THE HEARTBEAT

a. **Initiation of the Cardiac Impulse**. The initiation of the cardiac impulse begins in a highly specialized node of nervous tissue known as the sinoatrial node (also known as the SA node). As the name implies, the sino-atrial node is located in one of the atria-specifically the right atrium. The SA node initiates the electrical impulse that spreads out over both the atria causing the atrial muscles to contract. The fact that the SA node is located within the right atrium explains why the right atrium contracts 0.08 seconds before the left atrium contracts--although the contraction of the atria can still be considered to be simultaneous. As the atrial, muscle contracts the impulse travels through the atrial muscle to the atrioventricular (AV).node.

b. **Atrioventricular Node.** The AV node is located between the right atrium and the right ventricle. The AV node is responsible for the contraction of both the ventricles. From the atrioventricular node, the impulse travels through the Bundle of HIS to the purkinje fibers of the ventricles.

c. **Bundle of HIS.** The Bundle of HIS is a collection of cardiac fibers through which the impulse travels on its way to the Purkinje fiber system. The Bundle of HIS is located at the uppermost portion of the ventricular septum. The ventricular septum is the thick muscular membrane that separates the right ventricle from the left ventricle.

d. **Purkinje Fibers.** The Purkinje fibers transverse and branch off within the ventricular septum branching to supply both ventricles near the bottom of the septum. By branching close to the bottom of the ventricular septum, the contractions of the ventricles go in an upward direction that is necessary for proper blood flow. Consequently, the contraction of the ventricles forces the blood upward to the aorta and pulmonary arteries.

e. **Control of the SA Node and AV Node**. Both the SA and the AV node are controlled by the autonomic nervous system. Parasympathetic stimulation, supplied by the vagus nerve tends to decrease both the rate and force of contraction of the heart. Sympathetic stimulation, from the cervical sympathetic ganglia, serves to increase both the rate and force of contraction of the heart. The predominant sympathetic receptor is a beta-receptor although it has been shown that a small amount of alpha-receptors are present in the heart.

2-18. ELECTROLYTES OF SIGNIFICANCE IN HEART FUNCTIONING

As with all muscle and nervous tissue, a proper concentration of electrolytes is essential for normal heart function. The three electrolytes essential for proper cardiac function are potassium, calcium, and sodium.

a. **Potassium**. An increase in the level of potassium in the extracellular fluid causes a decrease in the heart rate as well as a decrease in the force of contraction. The heart becomes dilated and flaccid. An extremely large increase in potassium can block nervous conduction through the atrioventricular bundle. If potassium levels are increased two or three times above normal, the atrioventricular blockade is usually so severe that death occurs. Potassium depletion also causes a decrease in the heart rate and an increase in the force of contraction. This is of concern, especially in the patient who has been taking digitalis. As you will remember, digitalis is valuable in the treatment of heart failure because it decreases the heart rate as well as increases the force of contraction, thus the efficiency of the heart is increased. If potassium levels are depleted at too great a degree, digitalis intoxication can result in which case the heart rate might decrease to too slow a rate.

b. **Calcium**. Calcium is primarily involved with the contractile processes of the myocardium. An increase in calcium levels may cause over contraction of the heart and a decrease in calcium levels may cause cardiac flaccidity. It should be noted that calcium level alterations rarely reach the point where these effects can be seen.

c. **Sodium**. Sodium is another essential electrolyte involved in cardiac function. However, sodium imbalances are usually manifested in some of the other systems before cardiac problems arise. If sodium levels are increased above normal depressed cardiac function occurs. Sodium levels are of concern in congestive heart failure because of the edema that can certainly aggravate congestive heart failure. Persons having congestive heart failure must carefully monitor their sodium intake in that too much sodium can cause an excessive fluid accumulation in the tissues. This fluid accumulation causes the heart to work harder in order to compensate for the water.

d. **Magnesium.** Magnesium is an essential electrolyte involved as a cofactor in many enzyme systems. High magnesium levels may affect heart rate, cardiac conduction, and blood pressure. Hypotension, vasodilation, bradycardia, heard block and cardiac arrest can occur with increasing levels. Low magnesium may cause cardiac arrhythmias and may play an important role in atypical ventricular tachycardia (torsades de pointes). Magnesium is important in regulating intracellular potssium and calcium content and the movement of these cations is closely linked. Attempts to replace potassium is difficult if an existing magnesium or calcium deficiency is also present.

2-19. CARDIAC DISORDERS

Cardiac disorders are some of the top killers in the United States. A variety of medications are used in the treatment of these conditions.

a. **Bradycardia**. Bradycardia is a slow heart rate. Generally, bradycardia refers to a heart rate less than 60 beats per minute. This condition is sometimes referred to as sinus bradycardia because the decrease in heart rate is usually attributed to a decrease in the activity of the sinoatrial node. An increase in vagal tone is probably the cause of most cases of bradycardia. In most cases, bradycardia is not serious. Bradycardia is often observed in sleeping persons and in young athletes. There are no symptoms of bradycardia unless it is severe. For simple bradycardia, no treatment is usually needed; however, severe bradycardia may be treated with atropine.

b. **Tachycardia**. Tachycardia means a rapid heart rate. Generally, tachycardia refers to a heart rate more than 100 beats per minute. Tachycardia can be caused by a number of disorders (for example, hyperthyroidism, vagal suppression, sympathetic nervous system stimulation, emotional responses, and exercise). The usual treatment of tachycardia is aimed at removing its cause.

c. **Arrhythmia.** Arrhythmia is a term that is used to refer to any abnormal heartbeat (that is, missed beats or extra beats). There are two types of arrhythmias that will be discussed in this subcourse: flutter and fibrillation.

(1) Flutter. Flutter is a very rapid heart rate with rhythm present. Usually the heart rate is much faster than in simple tachycardia (between 200 to 400 beats per minute).

(2) Fibrillation. Fibrillation is a term which refers to an extremely rapid heart rate with no rhythm. This condition is treated with an electric defibrillator that reverses fibrillation with the use of an electric shock.

d. **Angina Pectoris**. Angina pectoris is an acute condition in which one or more of the coronary arteries becomes blocked. A sharp burning pain in the chest that may be felt also in the neck and left arm characterizes angina. The coronary arteries may become partially occluded (closed) by an embolism or thrombus, or a simple increase in oxygen demand when exercising, but is usually attributed to be a result of atherosclerotic obstruction of the coronary arteries. The heart muscle cells are thus deprived of oxygen because of the decreased flow of blood and death of the myocardial cells may result if the condition is not remedied. Acute management of angina pectoris is usually achieved with the use of a rapid acting vasodilator such as nitroglycerin or amyl nitrite.

e. **Myocardial Infarction**. A myocardial infarction is similar to angina pectoris, but it is usually more serious. During angina pectoris the coronary arteries are usually only partially blocked; however, during a myocardial infarction complete blockage of one of the coronary arteries results. The symptoms are essentially the same as angina pectoris, but are not usually relieved by vasodilators. Complete bed rest is essential for the patient. Death of cardiac muscle cells often results unless another vessel is able to carry blood to the affected area.

f. **Congestive Heart Failure**. Congestive heart failure is defined as a decrease in the efficiency of the pumping of the heart. This condition usually leads to pulmonary edema, a complication attributed to the fluid back up. Because of decreased blood flow, there is a decrease in renal circulation that can further aggravate the associated edema because of both decreased glomerular filtration rate and increased sodium retention. Vasodilators that belong to a class of drugs called Angiotensin Converting Enzyme Inhibitors (ACE inhibitors) are the first line drug of choice for treatment of congestive heart failure. If a patient cannot tolerate ACE inhbitors, they may be placed on a nitrate (Isordil) and hydralazine instead. As heart failure worsens and edema increases, diuretics are used to decrease edema. Digitalis glycosides (Digoxin) used to be the drug of choice for heart failure, however due to many drug-drug interactions and narrow therapeutic index, it is reserved for acute symptomatic heart failure or in patients with heart failure and atrial fibrillation. Digoxin works by increasing the efficiency of the heart as a pump by decreasing both the size of the heart and the rate of the heart while at the same time increasing the force of contraction. As heart failure worsens treatment may involves the addition of beta-adrenergic blockers (carvedilol, metoprolol) and spironolactone (potassium-sparing diuretic).

g. **Cardiac Arrest**. A cardiac arrest is simply the sudden cessation (stoppage) of the heartbeat. The cause of the stoppage may or may not be known. Treatment of the cardiac arrest is dependent upon the cause of the arrest.

h. **Rheumatic Fever**. Rheumatic fever is a streptococcal infection which many times attacks the valves of the heart. The result is a deformed or weakened valve that results in a heart murmur.

i. **Endocarditis**. Endocarditis is an inflammation of the membrane that lines the heart. Bacteria that repeatedly enter the bloodstream usually cause endocarditis. The bacteria that cause the endocarditis may enter the bloodstream following a tooth extraction and, on occasion, is associated with unsanitary intravenous injection techniques. Diagnosis of endocarditis usually involves the presence of a low fever and a soft, muffled heart murmur. The valves of the heart are also affected and if not detected and treated early endocarditis may cause irreversible damage. The treatment of endocarditis usually centers on bed rest and long term (4-6 weeks) antibiotic therapy.

j. **Heart Block**. A heart block is defined as a condition in which the cardiac excitation is slowed or interrupted somewhere in the normal pathway where conduction takes place. The two primary types of heart block usually seen are the SA or sinoatrial block and the atrioventricular or AV block. The term “heart block” is somewhat ambiguous. Usually the block only occurs occasionally and the result is manifested in only a skipped beat. Generally, the SA block requires no treatment; however, the prognosis is dependent on the cause and frequency of the block. During the AV block several or all impulses from the SA node are delayed or blocked in the AV node or bundle. Obviously, this type of block is much more serious than the SA block. Treatment of AV block depends upon the cause and the severity of the block. Digitalis toxicity may cause AV block on occasion.

2-20. CARDIOVASCULAR CIRCULATORY PATTERNS

See figure 2-4 for an illustration depicting cardiovascular circulatory patterns.

a. **General**. The human cardiovascular system is described as a closed, two-cycle system.

(1) It is closed because at no place is the blood as whole blood ever outside the system.

(2) It is two-cycle because the blood passes through the heart twice with each complete circuit of the body. In the pulmonary cycle, the blood passes from the right heart, through the lungs, and to the left heart. In the systemic cycle, the blood passes from the left heart, through the body in general, and returns to the right heart.

(3) It is common for an area of the body to be supplied by more than one blood vessel, so that if one is damaged, the others will continue the supply. This is known as collateral circulation. However, there are situations, such as in the heart and the brain, where a single artery supplies a specific part of a structure. Such an artery is called an end artery. When an end artery is damaged, the area supplied by it will usually die or be the cause of a “stroke” in the brain.

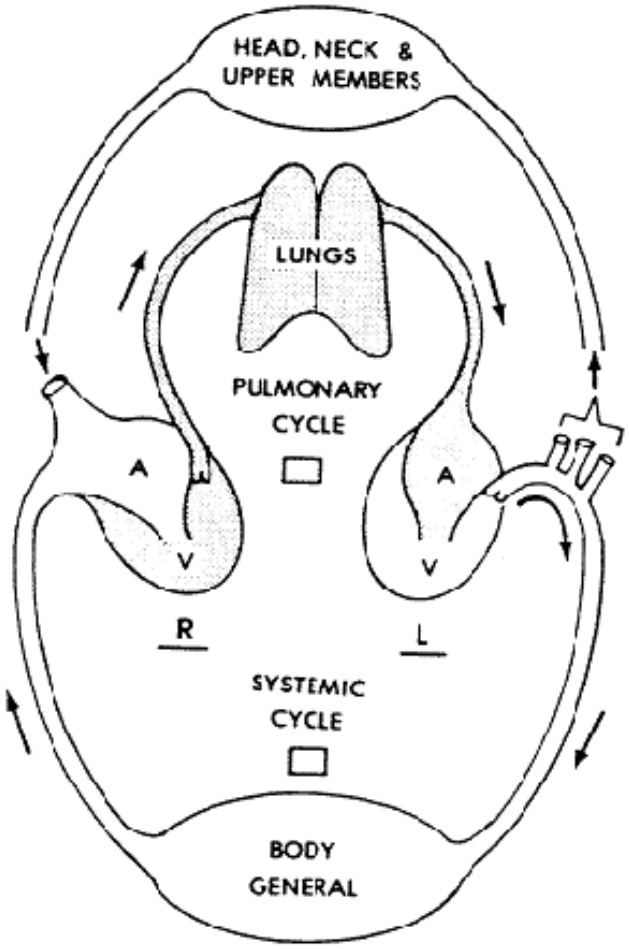


Figure 2-4. Cardiovascular circulatory pattern.

b. **Pulmonary Cycle**. The pulmonary cycle begins in the right ventricle of the heart. Contraction of the right ventricular wall applies pressure to the blood. This forces the tricuspid valve closed, and the closed valve prevents blood from going back into the right atrium. The pressure forces blood past the semilunar valve into the pulmonary trunk. Upon relaxation of the right ventricle, backpressure of the blood in the pulmonary trunk closes the pulmonary semilunar valve. The blood then passes into the lungs through the pulmonary arterial system. Gases are exchanged between the alveoli. This blood, now saturated with oxygen, is collected by the pulmonary veins and carried to the left atrium of the heart. This completes the pulmonary cycle.

c. **Systemic Cycle**.

(1) Left ventricle of the heart. The oxygen-saturated blood is moved from the left atrium into the left ventricle. When the left ventricular wall contracts, the pressure closes the mitral valve, which prevents blood from returning to the left atrium. The contraction of the left ventricular wall therefore forces the blood through the aortic semilunar valve into the aortic arch. Upon relaxation of the left ventricular valve, the back pressure of the aortic arch forces the aortic semilunar valve closed.

(2) Arterial distributions. The blood then passes through the various arteries to the tissues of the body. See figure 2-5 for an illustration of the main arteries of the human body.

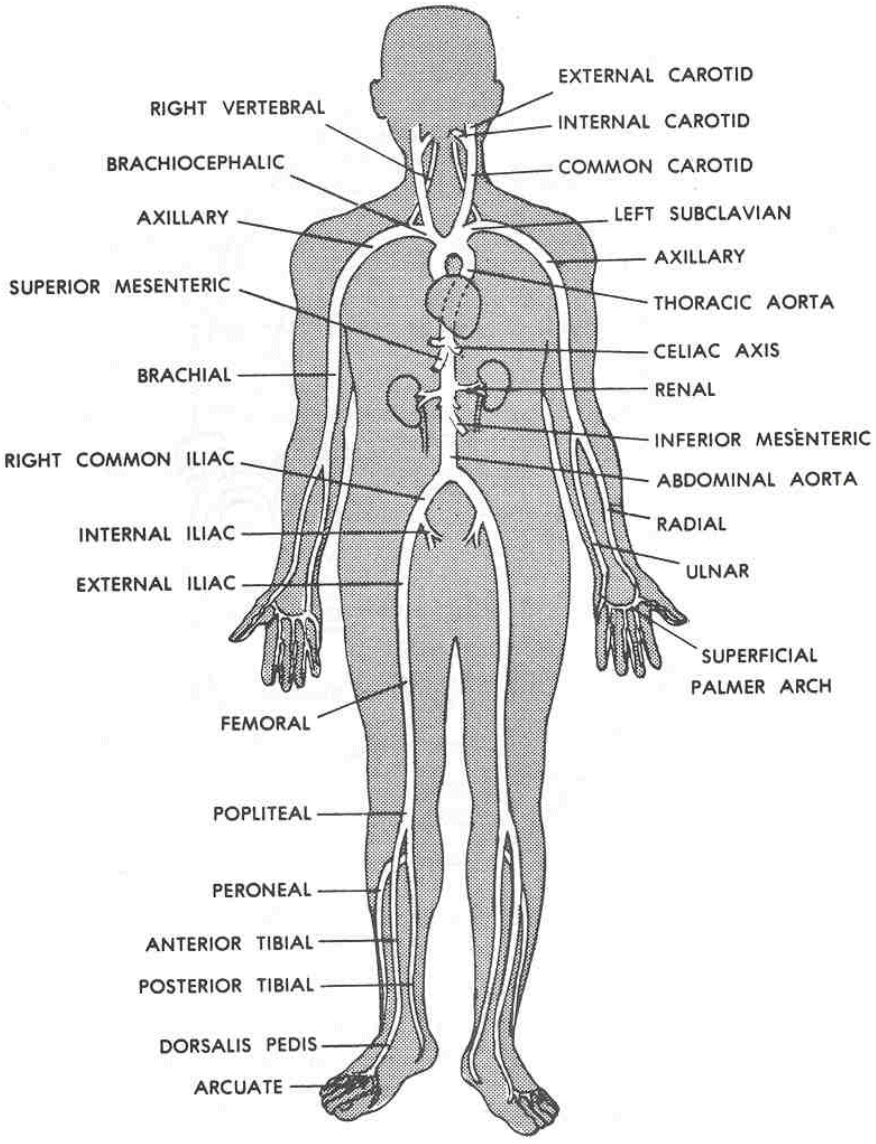


Figure 2-5. Main arteries of the human body.

(a) The carotid arteries supply the head. The neck and upper members are supplied by the subclavian arteries.

(b) The aortic arch continues as a large single vessel known as the aorta passing down through the trunk of the body in front of the vertebral column. It gives off branches to the trunk wall and to the contents of the trunk.

(c) At the lower end of the trunk, the aorta divides into right and left iliac arteries, supplying the pelvic region and lower members.

(3) Capillary beds of the body tissues. In the capillary beds of the tissues of the body, materials (such as food, oxygen, and waste products) are exchanged between the blood and the cells of the body.

(4) Venous tributaries. See figure 2-6 for an illustration of the main veins of the human body.

(a) The blood from the capillaries among the tissues is collected by a venous system parallel to the arteries. This system of deep veins returns the blood back to the right atrium of the heart.

(b) In the subcutaneous layer, immediately beneath the skin, is a network of superficial veins draining the skin areas. These superficial veins collect, and then join the deep veins in the axillae (armpits) and the inguinal region (groin).

(c) The superior vena cava collects the blood from the head, neck, and upper members. The inferior vena cava collects the blood from the rest of the body. As the final major veins, the venae cavae empty the returned blood into the right atrium of the heart.

(d) The veins are generally supplied with valves to assist in making the blood flow toward the heart. It is of some interest to note that the veins from the head do not contain valves.

(e) From that portion of the gut where materials are absorbed through the walls into the capillaries, the blood receives a great variety of substances. While most of these substances are useful, some may be harmful to the body. The blood carrying these substances is carried directly to the liver by the hepatic portal venous system. This blood is specially treated and conditioned in the liver before it is returned to the general circulation by way of the hepatic veins.

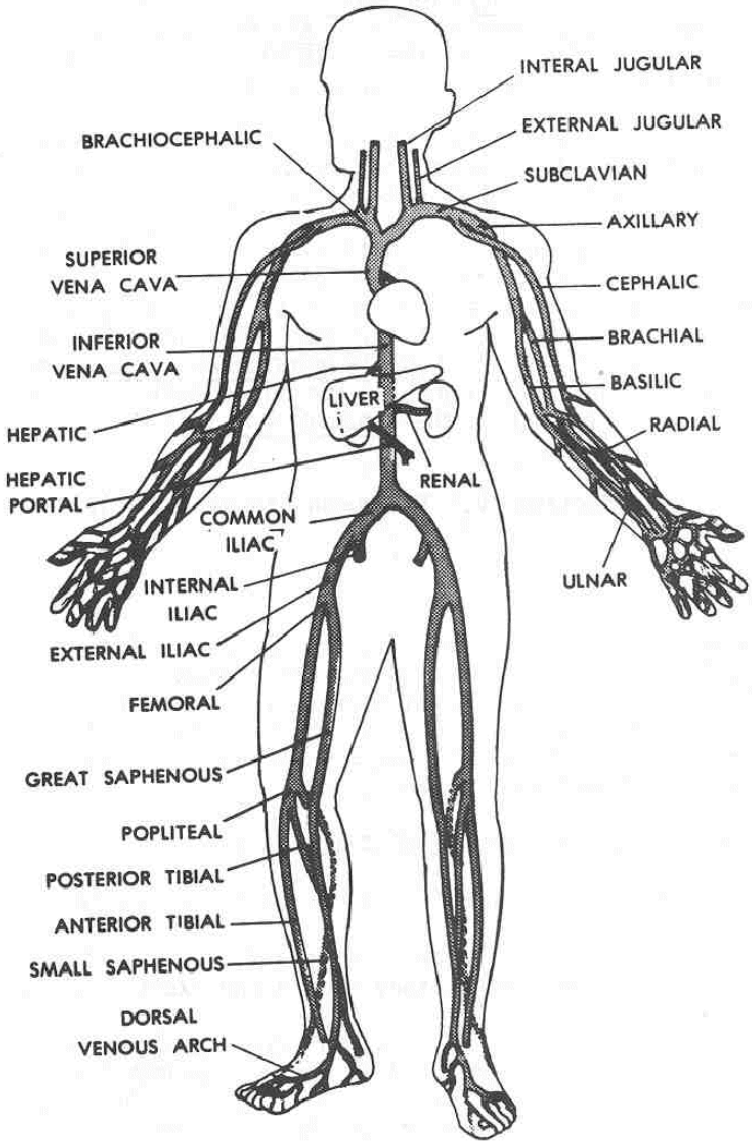


Figure 2-6. Main veins of the human body.

Section IV. THE HUMAN LYMPHATIC SYSTEM

2-21. GENERAL

Between the cells of the body are spaces filled with fluid. This is the interstitial (or tissue) fluid, often referred to as intercellular fluid. There are continuous exchanges between the intracellular fluid, the interstitial fluid, and the plasma of the blood. The lymphatic system returns to the bloodstream the excess interstitial fluid, which includes proteins and fluid derived from the blood.

2-22. STRUCTURES OF THE HUMAN LYMPHATIC SYSTEM

See figure 2-7 for an illustration of the human lymphatic system.

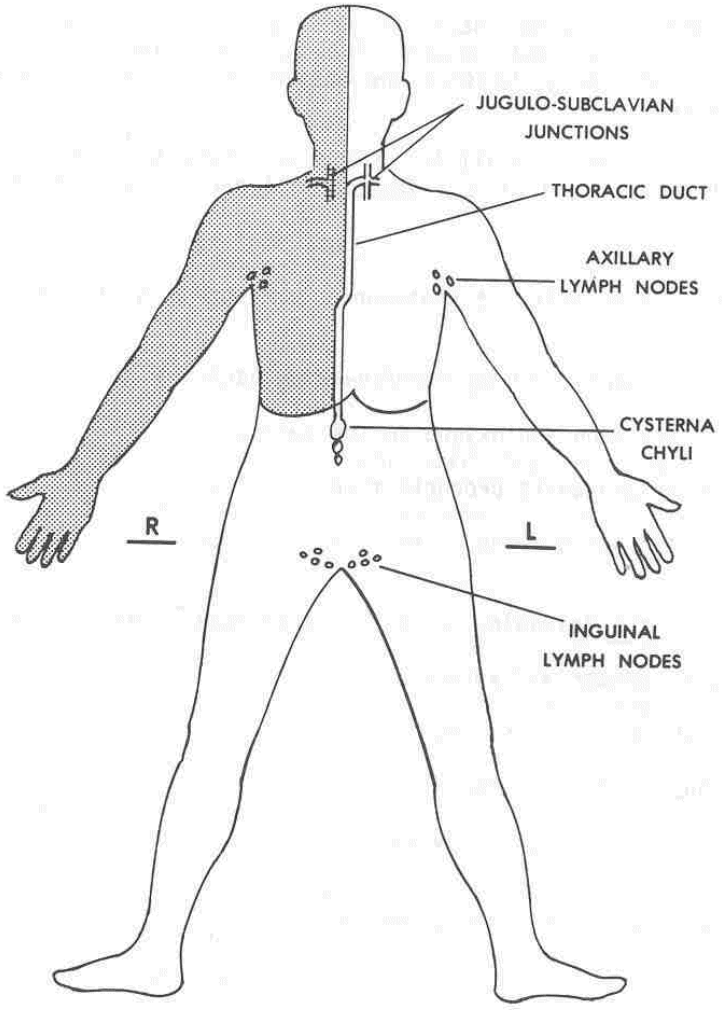


Figure 2-7. The human lymphatic system.

a. **Lymphatic Capillaries**. Lymphatic capillaries are located in the interstitial spaces. Here, they absorb the excess fluids.

b. **Lymph Vessels.** A tributary system of vessels collects these excess fluids, now called lymph. Like veins, lymphatic vessels are supplied with valves to help maintain a flow of lymph in one direction only. The lymphatic vessels, to a greater or lesser extent, parallel the venous vessels along the way. The major lymph vessel in the human body is called the thoracic duct. The thoracic duct passes from the abdomen up through the thorax and into the root of the neck in front of the vertebral column. The thoracic duct empties into the junction of the left subclavian and jugular veins.

c. **Lymph Nodes**. Along the way, lymphatic vessels are interrupted by special structures known as lymph nodes. These lymph nodes serve as special filters for the lymph fluid passing through.

d. **Tonsils**. Tonsils are special collections of lymphoid tissue, very similar to a group of lymph nodes. These are protective structures and are located primarily at the entrances of the respiratory and digestive systems.

Continue with Exercises

EXERCISES, LESSON 2

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. Which of the following statements best explain the need for circulatory systems?

   a. To protect the body from invading bacteria.

   b. To get food and oxygen to the cells.

   c. To remove waste products from the cells.

   d. To provide a means of cell reproduction.

2. Which of the following is a circulatory system in the human body? (More than one response may be correct.)

   a. The sinoatrial system.

   b. The lymphatic system.

   c. The diastolic system.

   d. The cardiovascular system.

3. Capillaries are best described as:

   a. Vehicles for nutrients, oxygen, and wastes.

   b. Very large conduits or channels through which the blood is moved.

   c. Very small vessels that provide exchange areas.

   d. The component of the cardiovascular system that serves as the primary motive force of blood movement.

4. Which of the following is a component of the blood?

    a. Plasma.

    b. Formed elements (red blood cells, white blood cells, and platelets).

    c. Both a and b.

5. Plasma is best described as:

    a. The protein material that carries dissolved oxygen in the blood.

    b. The liquid portion of the blood that is responsible for blood clotting.

    c. The clear fluid that remains after the blood has clotted.

    d. The clear fluid portion of the blood that accounts for approximately 55 percent of the total blood volume.

6. Red blood cells (RBCs) are best described as:

    a. Fragments of cells that aid in the clotting of blood by clumping together and by releasing certain chemical factors related to clotting.

    b. The formed elements of the blood that phagocytize (swallow up) foreign particles and organisms.

    c. Biconcave discs that contain hemoglobin, a protein responsible for carrying most of the oxygen transported by the blood.

    d. The formed elements of the blood that produce antibodies and serve other functions in immunity.

7. Which of the following statements best describes veins?

    a. The blood vessels that carry blood to the chambers of the heart.

    b. The blood vessels that carry blood away from the chambers of the heart.

    c. Extremely thin-walled blood vessels that act as exchange areas.

    d. Blood vessels that always carry deoxygenated blood.

8. Below are the steps involved in the clotting of blood. Select the arrangement of steps that best reflects their sequential order in the clotting process.

    I. Thromboplastin reacts with calcium and another substance, prothrombin, to form thrombin.

    II. The blood platelets release a substance that is known as thromboplastin.

    III. The thrombin formed acts as an enzyme to convert fibrinogen to fibrin threads that eventually form the blood clot.

    a. I, II, and III.

    b. III, II, and I.

    c. II, III, and I.

    d. II, I, and III.

9. Blood pressure is best described as:

    a. The residual pressure of the blood due to the elasticity of the blood vessels.

    b. The force exerted by the blood as it is pumped throughout the circulatory system.

    c. The pressure the blood exerts as it is pumped from the heart.

    d. The pressure the blood exerts when the heart is resting.

10. Which of the following is a medical problem associated with high blood pressure?

    a. Frequent nosebleeds.

    b. Arteriosclerosis.

    c. Strokes.

    d. Hypertrophy of the myocardium.

    e. All of the above.

11. Hemophilia is:

    a. A very serious type of anemia characterized by a progressive degeneration of the bone marrow.

    b. A hereditary disease characterized by a lack of one of the factors necessary for the clotting of the blood.

    c. A general term that refers to a group of anemias caused by weakened red blood cell membranes.

    d. A type of anemia caused by a deficiency of elemental iron in the blood.

12. Leukemia is:

    a. A very serious and usually fatal condition characterized by the excessive production of red blood cells.

    b. A serious type of anemia predominant in older people because they tend to have red blood cells with weakened membranes.

    c. A disease of the white blood cell forming tissue characterized by an abnormally high white blood cell count.

    d. A disease of the red blood cell forming tissue which results in the production of excessive numbers of red blood cells which phagocytize the other cells in the blood.

13. Arteriosclerosis is:

    a. A condition characterized by a loss of elasticity or hardening of the arterial walls.

    b. A condition characterized by vasoconstriction of the arteries in the extremities.

    c. A condition that occurs when a clot is formed in a blood vessel.

    d. A serious condition that affects the arteries and causes them to lose vital fluids.

14. Which of the following statements best describes the property inherent rhythmicity?

    a. The property of cardiac cells which allows them to beat without the presence of any electrolytes.

    b. The property of the heart cells that allows them to initiate each contractile process instead of requiring them to govern the rate of the heart beat.

    c. The property of the myocardium to continue pumping blood after the individual has died.

    d. The property of the cardiac muscle that allows cardiac muscle cells to beat separately without any stimulation.

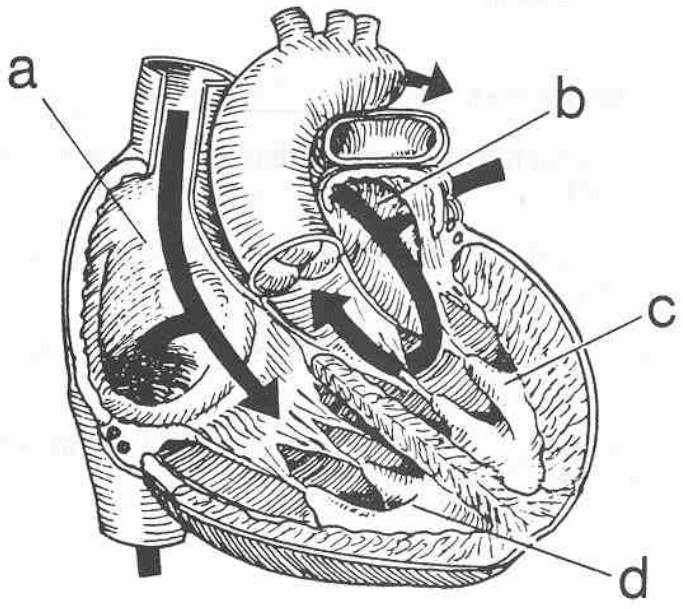
15. Match the name of each part of the heart with its respective structure.

    _____ Left atrium.

    _____ Right atrium.

    _____ Left ventricle.

    _____ Right ventricle.



16. Which statement best describes the role of the Bundle of HIS in the heartbeat?

    a. The Bundle of HIS is responsible for the contraction of both the ventricles.

    b. The Bundle of HIS is a collection of cardiac fibers through which the impulse travels on its way to the Purkinje fibers.

    c. The Bundle of HIS provides nervous stimulation so that the ventricles go in a downward direction, which is necessary for proper blood flow.

    d. The Bundle of HIS is responsible for initiating the cardiac impulse.

17. What is the effect of excessive levels of calcium in the extracellular fluid?

    a. Cardiac flaccidity.

    b. Cardiac edema.

    c. Spastic condition of the heart.

    d. A decrease in the force of contraction of the heart beat.

18. Congestive heart failure is best described as:

    a. An acute condition in which one or more of the coronary arteries become blocked.

    b. A complete blockage of one or more of the coronary arteries which results in damage to the cardiac muscle.

    c. An inflammation of the membrane that lines the heart.

    d. A decrease in the efficiency of the pumping of the heart which usually leads to pulmonary edema.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 2

1. b (para 2-1b)
   c (para 2-1b)

2. b (para 2-3b)
   d (para 2-3a)

3. c (para 2-4d)

4. c (para 2-5)

5. d (para 2-5a)

6. c (para 2-5b(1))

7. a (para 2-6b(2))

8. d (para 2-8)

9. b (para 2-9a)

10. e (para 2-10a)

11. b (para 2-11e)

12. c (para 2-11f)

13. a (para 2-13a)

14. d (para 2-16a)

15. b Left atrium. (figure 2-2)
    a Right atrium. (figure 2-2)
    c Left ventricle. (figure 2-2)
    d Right ventricle. (figure 2-2)

16. b (para 2-17c)

17. c (para 2-18b)

18. d (para 2-19f)

End of Lesson 2

LESSON ASSIGNMENT

SUBCOURSE MD0806 Therapeutics III.

LESSON 3 Cardiac Drugs.

LESSON ASSIGNMENT Paragraphs 3-1--3-15.

OBJECTIVES After you finish this lesson you should be able to:

3-1. From a group of statements, select the best description of congestive heart failure.

3-2. Given a group of statements, select the statement which best describes the primary pharmacological property of digitalis and related cardiac glycosides.

3-3. Given a group of statements, select the statement which best describes digitalizing dose.

3-4. From a group of statements, select the statement that best describes the difference between the digitalizing dose and the maintenance dose of digitalis.

3-5. Given the trade and/or generic name of a cardiac drug and a group of uses, side effects, or patient precautionary statements, select the use(s), side effect(s), or patient precautionary statement(s) for that drug.

3-6. Given the trade or generic name of a cardiac agent and a group of drug names (trade and/or generic), select the corresponding trade or generic name for the given drug.

3-7. Given a group of statements and one of the following terms: cardiac arrhythmia flutter or fibrillation, select the statement which best defines the given

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 3

CARDIAC DRUGS

Section I. CONGESTIVE HEART FAILURE AND ITS TREATMENT

3-1. INTRODUCTION

Heart disease is the number one killer in the United States today. Two people succumb to conditions related to heart disease every minute of the day. However, it must be remembered that heart disease can be treated. Discoveries of new ways to use existing drugs and improved surgical techniques translate into longer and more productive lives for persons who have heart disease. In lesson 2 of this subcourse, various disease states that can affect the circulatory system were discussed. In this lesson, some of these conditions will be reviewed. The primary focus of this lesson will be the drug used to treat these conditions.

3-2. REVIEW OF CONGESTIVE HEART FAILURE

Congestive heart failure may be defined as nonefficient pumping of the heart. This inefficiency in pumping the heart leads to an increase in the size of the heart and an increase in the heart rate. This increase in heart size and heart rate result because of the heart's attempt to compensate for the poor efficiency in pumping blood to other parts of the body. Consequently, the kidneys improperly function. Improperly functioning kidneys result in edema of the extremities due to improper excretion (removal) of sodium and waste products in the urine. If a patient's congestive heart failure becomes acute, he may have pulmonary edema due to poor kidney function.

3-3. TREATMENT OF CONGESTIVE HEART FAILURE

Rest and restriction of sodium (sodium chloride) intake are important aspects of the non-pharmacologic treatment of congestive heart failure. Drug treatment includes ACE inhibitors, diuretics (see Lesson 8), digitalis and the related cardiac glycosides, beta adrenergic blockers, and spironolactone.

3-4. ANGIOTENSIN-CONVERTING ENZYME INHIBITORS (ACE INHIBITORS)

a. Angiotensin-converting enzyme inhibitors (ACE inhibitors) belong to a unique class of vasodilators. ACE inhibitors block a specific enzyme (angiotensin converting enzyme) that converts angiotensin I to angiotensin II. Angiotensin II is one of the most potent vasodilators in the body. The mechanism of action of ACE inhibitors in the treatment of congestive heart failure relies on the ability to cause both aterial and venous vasodilation through this inhibition, thereby decreasing the workload on the heart. Hemodynamic effects associated with long term use include increased cardiac function and a decrease in blood pressure and heart rate. Significant improvements are seen in exercise tolerance and left ventricular size. ACE inhibitors are well tolerated and have been show to decrease hospitalizations and deaths. For these reasons, agents in this class are first line pharmacologic treatment for congestive heart failure.

b. ACE inhibitors are often initiated immediately after a heart attack or when a patient still has mild symptoms of heart failure. The starting dose is low and titrated (gradually increased) up to the maximum tolerated dose (based on heart rate and blood pressure). The most bothersome side effect is a dry cough that develops in some patients. Other side effects include angioedema (facial swelling) and elevated potassium levels.

c. Agents included in this class include captopril (Capoten®), enalapril (Vasotec®), lisinopril (Prinivil®, Zestril®), and ramipril (Altace®)

3-5. DIGITALIS AND THE RELATED GLYCOSIDES

a. The mechanisms of action of digitalis and related cardiac glycosides in the treatment of congestive heart failure are not fully understood. The main pharmacological property of these drugs is their ability to increase the force of myocardial contraction (the heart muscle's contraction) by a direct action on the ventricular heart muscles. Conduction is also slowed somehow between the SA node and the AV node, resulting in a decrease in heart rate. Because of the slower heart rate and increase in the force of the myocardial contraction, the heart has more time to adequately fill with venous blood. The secondary changes seen as a result of the first three mechanisms of action will be a decrease in heart size and a decrease in heart rate due to more efficient pumping of the heart. Because of the slower heart rate, cardiac glycosides are also used in the treatment of atrial flutter and atrial fibrillation.

b. Because of improved circulation to the kidneys, an increase in urinary output (diuresis) within 24 to 48 hours following administration of cardiac glycosides will also be seen. Digitalis toxicity is enhanced in patients who have low serum potassium (hypokalemia), so potassium supplements may be given based upon periodic blood test analysis.

c. Digitalis and related glycosides have very narrow therapeutic indices (the treatment dose is very close to the toxic dose) and many drug-drug interactions. The dose must also be adjusted in renal failure, which is common in congestive heart failure (CHF) patients. For these reasons digitalis is reserved for acute symptomatic heart failure or in those patients with CHF and atrial fibrillation.

3-6. DIGITALIZING DOSE

a. The digitalizing dose of a cardiac glycoside is the initial large dose of the drug that is given to the patient in order to relieve the symptoms of congestive heart failure or to render the patient asymptomatic as it is commonly referred to. Often the digitalization is accomplished by administering relatively large doses of digitalis preparations within 18 to 24 hours to the patient. This type of intensive administration of "loading" doses can cause toxic reactions since digitalis preparations have only a moderate safety margin.

b. Although a patient's condition may have responded to digitalization, he may have to continue to take a digitalis product for a long period. The physician must determine the amount of drug the patient must take on a daily basis in order for the patient's heart to perform at its optimal level. Maintenance doses are ordered which are just enough to replace the amount of digitalis eliminated since the administration of the last dose. The maintenance dose is then taken each day to maintain the quantity of drug required to keep the patient's heart beating efficiently. Although these daily maintenance doses are much lower than the original digitalizing doses, the risk of toxicity remains.

3-7. DIGITALIS PRODUCTS

a. **Digoxin (Lanoxin®).** Digoxin is the most common cardiac glycoside used to treat congestive heart failure. The drug is usually administered intravenously (IV) for digitalization in a total dosage of from 1 to 1.5 milligrams. This drug may be given orally if the physician desires. The maintenance dose ranges from 0.125 milligram to 0.5 milligram daily, but normally 0.25 milligram of digoxin is given each day to the patient. The side effects of digoxin include anorexia (loss of appetite), arrhythmias, nausea and vomiting, and yellowish-green vision. Digoxin should be used with caution in patients who have kidney problems because the kidneys are the primary route of excretion for this agent. This drug should be used with caution in patients who have low serum potassium. Digoxin is available in 0.125 milligram, 0.25 milligram, and 0.5 milligram tablets; 0.05 milligram, 0.1milligram and 0.2mg liquid filled capsules; or in an injectable solution of 0.1 milligram per milliliter in 1 milliliter containers and 0.25 milligram per milliliter in 2 milliliter containers. It is also available in a 0.05 milligram per milliliter pediatric elixir. The bioavailability is improved with the liquid filled capsules such that 0.1mg of the capsule is equivalent to 0.125mg of the tablet. Many times the physician will prescribe the pediatric elixir with directions for the patient to take a certain total daily dose (e.g., 0.125 milligram). You must interpret this as milliliters (or cubic centimeters-

cc's) in order for the patient to dose himself with the calibrated dropper supplied with the preparation. As you probably realize, you might have to use your pharmaceutical calculation skills to calculate the dose of the drug solution.

b. **Digitoxin (Crystodigin®).** Digitoxin is another cardiac glycoside obtained from Digitalis purpurea. Although rarely used, you must be aware of this agent as it can be confused with digoxin. This product must be used with caution in patients with liver problems since this drug is excreted primarily in the bile and consequently, has a long half-life (5 to 7 days). The drug is available as a 0.1 mg and 0.2mg tablet.

3-8. OTHER AGENTS USED IN CONGESTIVE HEART FAILURE

a. **Beta Adrenergic Blocking Agents.** The stimulation of beta-1 receptors in cardiac tissue causes an increase heart rate often causing an increase in workload of the heart. As heart failure worsens, the body compensates by stimulating beta receptors to make the heart pump faster and faster. Consequently, the faster the heart pumps, the less time the ventricles have to fill and pump efficiently. Beta adrenergic blocking agents work by blocking this stimulation and allowing less work by the heart by decreasing the heart rate. Doses are initiated very low and titrated very slowly (over weeks to months). Large initial doses of beta blockers will actually worsen the patient's condition and produce heart failure. The most common agents used in the treatment of heart failure include carvedilol (Coreg®) and metoprolol (Lopressor®).

b. **Spironolactone (Aldactone®).** Spironolactone is a potassium sparing diuretic that works by inhibiting aldosterone and causing diuresis. It is useful in the treatment of edema common in CHF patients.

c. **Amiodarone (Cordarone®).** Amiodarone is an agent used in the treatment of atrial and ventricular arrhythmias. However, when used in patients that have CHF and arrhythmias, it has been shown to improve exercise tolerance, decrease hospitalizations, and improve pump function.

Section II. THE ANTIARRHYTHMIC AGENTS

3-9. REVIEW OF CARDIAC ARRHYTHMIAS

Disorders of impulse information, impulse conduction, or a combination of these factors produce cardiac arrhythmias (or abnormal heartbeats). These are two types of arrhythmias that we will consider: flutter and fibrillation.

a. **Flutter**. Flutter is a very rapid heart rate with rhythm present. Usually the heart rate is much faster in flutter than it is in simple tachycardia. In flutter, the heart can beat from 200 to 400 beats per minute.

b. **Fibrillation**. Fibrillation occurs when there is a very rapid heart beat with no rhythm.

3-10. THE USE OF ANTIARRHYTHMIC DRUGS

The term antiarrhythmic drugs refer to the agents that suppress abnormal beats or restore normal cardiac rhythm by depressing various properties of the myocardium (heart muscle). This is a general mechanism of action for all these drugs. The toxicity of the drugs will be discussed with each individual drug since it varies with each agent.

3-11. SPECIFIC ANTIARRHYTHMIC DRUGS

a. **Quinidine (Quiniglute®, Quinidex®).** Quinidine is an antiarrhythmic agent used in the treatment of atrial fibrillation and ventricular arrhythmias. It is given orally in a usual dose of 200 to 400 milligrams every 6 to 8 hours. The side effects associated with quinidine include hypersensitivity reactions, gastrointestinal (GI) disturbances (nausea, vomiting, and diarrhea) and a group of symptoms known as cinchonism. Some symptoms associated with cinchonism are tinnitus (ringing in the ears), vertigo (dizziness), and headaches.

b. **Procainamide (Pronestyl®).** Procainamide is used in the treatment of atrial and ventricular arrhythmias in an oral dosage range of from 250 to 500 milligrams four times daily. Procainamide is similar in chemical structure to procaine. It retains the quinidine like actions of procaine, but it is not rapidly hydrolyzed and its action persists long enough so that it is active even after oral as well as parenteral administration. Pharmacologically, procainamide is equivalent to quinidine. Procainamide may cause anorexia, nausea and vomiting, and drug hypersensitivity.

c. **Propranolol (Inderal®).** Propranolol is an agent that is used in the treatment of hypertension, angina pectoris, and cardiac arrhythmias. It is especially useful in the treatment of ventricular arrhythmias. The normal dosage of this drug for antiarrhythmic purposes is 10 to 40 milligrams given three or four times daily. As you might expect, the dose of the drug can be adjusted to meet the individual needs of the patient. The side effects associated with propranolol include bradycardia, bronchoconstriction, and congestive heart failure (CHF). These arise because of the beta blocking effects of the drug. The drug should be used with caution in persons who have asthma. Other commonly used beta blocking agents include metoprolol (Lopressor®), atenolol (Tenormin®), and sotalol (Betapace®).

d. **Phenytoin (Dilantin®).** Phenytoin is an agent that may be administered intravenously to reverse digitalis-induced arrhythmias. Rapid intravenous administration may cause bradycardia, hypotension, and cardiac arrest (rarely).

e. **Lidocaine (Xylocaine®).** Lidocaine is an agent that may be given intravenously in the treatment of ventricular arrhythmias. Large intravenous doses may produce convulsions, coma, and respiratory depression. You should be aware that not all lidocaine solutions are to be administered intravenously. Lidocaine for intravenous use is clearly marked as such on the container.

f. **Amiodarone (Cordarone®).** Amiodarone is an agent that is used to treat life-threatening ventricular arrhythmias and occasionally atrial arrhythmias. It is administered as an IV loading dose over 24 hours followed by oral maintenance. Use of amiodarone is associated with hepatic, ophthalmic, thyroid, and pulmonary side effects.

g. **Diltiazem (Cardizem®).** Diltiazem is used intravenously (5-20 mg/hr) to control ventricular rate in atrial flutter or fibrillation. The oral dosage is 240 mg to 320 mg per day in divided doses 1 to 4 times daily. Side effects include hypotension, bradycardia, congestive heart failure (CHF), edema, and dermatitis.

Section III. ANTIHYPERLIPIDEMIC AGENTS

3-12. REVIEW OF ATHEROSCLEROSIS.

Atherosclerosis is a condition in which lipid (fat) deposits form on the inside of the arteries causing a decrease in the flow of blood through the arteries. The make up of these deposits is mostly cholesterol as a consequence of genetic and dietary factors which result in too much cholesterol. The arteries of most concern are the coronary arteries (those that supply the heart) and the carotid arteries (those that supply the brain). Hyperlipidemia is a condition of high levels of cholesterol, triglycerides, and/or lipoprotein in the blood. The higher the levels in the blood, the greater the risk that they will form deposits on the inside of arteries. Several studies have shown a correlation between cholesterol levels and premature heart disease. Studies have shown that each one percent reduction in serum cholesterol correlates with a two percent decline in the risk of myocardial infarction. For example, a 25 percent reduction in cholesterol will reduce the risk of myocardial infarction by 50 percent. Diet, exercise, antihyperlipidemic drugs, and surgery are the most common treatments. If a patient has high cholesterol only and no evidence of atherosclerosis, the treatment of the hyperlipidemia is referred to as primary prevention. If the patient already has atherosclerosis, treatment is known as secondary prevention.

3-13. DEFINITIONS

a. **Cholesterol**. Cholesterol is a fat-related compound. It is a normal constituent of bile and a principal constituent of gallstones. In body metabolism cholesterol is important as a precursor of various steroid hormones such as sex hormones and adrenal corticoids. Cholesterol is synthesized by the liver. It is widely distributed in nature, especially in animal tissue such as glandular meats and egg yolk.

b. **Triglyceride**. Triglyceride (TG) is a compound of three fatty acids esterified to glycerol. It is a neutral fat synthesized from carbohydrate and stored in adipose tissue. It releases free fatty acids into the blood on being hydrolyzed by enzymes.

c. **Lipoproteins**. Lipoproteins are fat with protein. Major carriers of lipids in the plasma are listed below.

(1) Chylomicron. Chylomicron is a particle of fat - lipoprotein - appearing in the lymph and blood after a meal rich in fat. These particles are composed largely of triglycerides with lesser amounts of phospholipids, cholesterol, esters, and protein. About 2 to 3 hours after a fat meal, the chylomicrons cause lactescene (milkiness) in the blood plasma; this is termed alimentary lipemia.

(2) Very low-density lipoprotein (VLDL). VLDL carries a large lipid (TG) content, but includes about 10 to 15 percent cholesterol. They are formed in the liver from endogenous fat sources.

(3). Intermediate-density lipoprotein (IDL). IDL continues the delivery of endogenous TG to cells and carries about 30 percent cholesterol.

(4) Low-density lipoprotein (LDL). LDL carries, in addition to other lipids, about two thirds or more of the total plasma cholesterol. It is formed in the serum from catabolism of VLDL. Because LDL carries cholesterol to the cells for deposit in the tissues, it is considered the main agent of concern in elevated serum cholesterol levels.

(5) High-density Lipoprotein (HDL). HDL carries less total lipid and more protein. It is also formed in the liver from endogenous fat sources. Because HDL carries cholesterol from the tissues to the liver for catabolism and excretion, higher serum levels are considered protective against cardiovascular disease.

3-14. RISK FACTORS

Although high cholesterol levels are a risk factor for the development of atherosclerosis, it is not the only risk factor. How aggressively the health care provider decides to treat hyperlipidemia depends on the patient's overall risk for developing atherosclerosis (heart disease). In addition to hyperlipidemia, the following are significant risk factors.

a. **Uncontrollable Risk Factors**. Uncontrollable risk factors include age (greater than 45 for males and greater than 55 for females), sex (male), and family history of premature coronary heart disease (MI, stroke or sudden death before age 55 male parent or sibling, 65 in female a parent or sibling).

b. **Controllable Risk Factors**. Controllable risk factors include active tobacco smoking, hypertension (treated or untreated), diabetes, severe obesity (more than 30 percent overweight), physical inactivity, and Type A personality traits.

NOTE: A high HDL (greaten than 60 mg/dl) is actually considered a *negative risk factor.* This means one positive risk factor may be subtracted in overall risk assessment. When determining treatment, two or more risk factors are considered significant.

3-15. TREATMENT

The treatment of hyperlipidemia depends on whether that patient has existing atherosclerosis and the patient's other risk factors for atherosclerosis. The treatment goal is usually expressed at the low-density lipoprotein (LDL) goal as this is the major carrier of cholesterol in the blood. See table 3-1.

CATEGORY	***LDL-CHOLESTEROL GOAL***
No atherosclerosis and less than two risk factors	*<160 mg/dl*
No atherosclerosis and two or more risk factors	*<130 mg/dl*
Existing atherosclerosis	*<100 mg/dl*

Table 3-1. Treatment goals.

a. **Diet and Exercise**. Diet and exercise are considered lifestyle modifications which may lower cholesterol levels to goal. Diet changes reduce intake of cholesterol and fat, especially saturated fat. Exercise may involve aerobic exercise for at least 20 to 30 minutes, 3 to 5 times weekly. Whether a patient is on medication to lower their cholesterol or not, diet and exercise should always be a part of the treatment regimen.

b. **Drug therapy.** Medications are often prescribed for hyperlipidemia when diet and exercise fail to normalize LDL levels. Agents may prevent cholesterol synthesis or promote the breakdown of internal cholesterol.

(1) Statins**.** Statins are also called HMG CoA (hydro-methylglutaryl coenzyme A) reductase inhibitors. HMG CoA is needed to produce mevalonic acid in the body that is used to produce many products; among them, cholesterol. As cholesterol synthesis is inhibited, LDL receptor site production is increased to draw cholesterol from serum. All of the statins work the same, but may differ in potency (degree to which they decrease cholesterol levels). The more potent statins may significantly reduce triglycerides as well as LDL. Some agents may increase HDL (this is good!). Because the liver makes most of our cholesterol at night, these agents work best when administered at bedtime. The most common side effects include muscle aches and weakness, diarrhea, constipation, and headache. Generalized muscle aches (over the entire body) must be reported immediately as this may indicate a more serious condition. Common statins include cerivastatin (Baycol®), simvastatin (Zocor®), atorvastatin (Lipitor®), and pravastatin (Pravachol®).

(2) Resins. Resins, also known as bile acid sequestrants, bind to bile acids in the GI tract and cause the break down of internally produced cholesterol, thus lowering cholesterol levels. Resins may increase triglyceride levels, so they must be used with caution in patients that have high triglycerides. Resins are very effective, however, patients express poor compliance with these agents due to the side effects of heatburn, nausea, flatulence, constipation, dosing regimens, and significant drug-drug interactions. Resins are positively charged and many medications that carry a negative charge will bind with them. Medications such as digoxin, thiazide diuretics, betablockers, warfarin, thyroxine and fat-soluble vitamins (A,D,K, and folic acid) should not be taken after these agents. If a patient is prescribed a resin, he should take other medications 2 hours before or 4 hours after the resin. These agents are in the form of a powder (must be mixed with juice) or very large tablet. Commonly prescribed resins include colestipol (Colestid®) and cholestryamine (Questran®).

(3) Fibrates. Fibrates are use primarily used to treat high triglyceride levels. They also increase HDL significantly and their effect on LDL varies. Side effects include nausea, flatulence, abdominal pain, and diarrhea. While on this medication, there is two to four percent increase in risk of developing gallstones. This medication should not be taken with HMG CoA enzyme inhibitors as there is the potential for development of severe muscle aches and weakness (myopathy). Fibrates include gemfibrozil (Lopid®) and fenofibrate (Tricor®).

(4) Nicotinic acid derivatives. Nicotinic acid derivatives (niacin, vitamin B_3) are used for reducing high LDLs and triglycerides. They are also useful for treating low HDL levels. As with fibrates, HMG CoA reductase inhibitors should be avoided as the combination will lead to a serum increase of HMG CoA and myopathy. The classic side effect of niacin is facial redness and flushing. Often, aspirin is administered 30 minutes prior to the niacin dose or niacin is initiated at low doses and gradually increased to reduce this side effect. Other side effects include headache, gastrointestinal upset, and dizziness. Only about 50 to 60 percent of patients can tolerate niacin because of its side effects. Some other side effects are itching, rashes, hepatotoxicity, elevated glucose levels, and gout. Niacin is relatively contraindicated in diabetics, patients with gout, and patients with peptic ulcer disease.

Continue with Exercises

EXERCISES, LESSON 3

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. From the statements below, select the statement that best describes congestive heart failure (CHF).

   a. Congestive heart failure is nonefficient pumping of the heart that leads to an increase in the heart size and heart rate.

   b. Congestive heart failure is a condition in which there is a build-up of edema in the extremities because of too forceful contractions of the myocardium.

   c. Congestive heart failure is a condition in which the heart fills with fluid after each contraction.

   d. Congestive heart failure is a state in which the heart valves open and close at inappropriate times resulting in backflow into the lungs.

2. Which of the following statements best describes the term digitalizing dose?

   a. The dose of digitalis required on a daily basis to prevent the patient from having the signs and symptoms of congestive heart failure.

   b. The large dose of digitalis which is first given to the patient in order to prevent cardiac arrhythmias.

   c. The digitalizing dose is the large initial dose of the drug that is given to the patient in order to relieve the symptoms of congestive heart failure.

   d. The large doses of digitalis that are frequently administered to patients who have acute cases of congestive heart failure.

3. The primary difference between the digitalizing dose and the maintenance dose of digitalis is:

    a. The digitalizing dose is the first and largest dose given to the patient, while the maintenance dose is the amount of drug given to the patient on a daily basis.

    b. The digitalizing dose is always smaller than the daily maintenance dose that is given to the patient.

    c. The digitalizing dose is the amount of digitalis given to the patient during the first three weeks of therapy, while the maintenance dose is given thereafter.

    d. The digitalizing dose is given to patients, who have acute CHF, while the maintenance dose is given to only those patients who must continue to take digitalis for the rest of their lives.

4. Phenytoin can be administered intravenously to treat

    a. Congestive heart failure.

    b. Digitalis induced arrhythmias.

    c. Cinchonism.

    d. Anorexia.

5. Inderal® is an agent used in the treatment of hypertension, angina pectoris, and:

    a. Cinchonism.

    b. Cardiac arrhythmias.

    c. Urine retention.

    d. Diarrhea.

6. Amiodarone is used in the treatment of:

    a. Cinchonism.

    b. Anorexia.

    c. Ventricular arrhythmias.

    d. Hypertension.

7. A side effect associated with the use of Zestril® is:

    a. Edema of the left ventricle.

    b. Localized analgesia.

    c. Dry cough.

    d. Postural hypotension.

8. One of the side effects associated with large initial doses of beta blocking agents is:

    a. Anemia.

    b. Hypertension.

    c. Ventricular arrhythmias.

    d. Congestive heart failure.

9. Flutter is best described as:

    a. A rapid heart beat with no rhythm.

    b. A rapid heart rate of at least 200 to 400 beats per minute.

    c. A type of cardiac arrest characterized by pain in the right shoulder.

    d. A very rapid heart beat with rhythm present.

10. Hyperlipidemia is best described as:

    a. Elevated levels of cholesterol, triglycerides, and/or lipoproteins in the blood.

    b. Reduced levels of cholesterol in the blood.

    c. Reduced levels of triglycerides in the blood.

    d. Elevated levels of triglycerides in the blood.

11. The following are acceptable treatments for hyperlipidemia:

    a. Diet and exercise

    b. Drug therapy

    c. Surgical intervention.

    d. All of the above.

12. Match the generic in Column A with its corresponding trade name in Column B.

Column A		Column B
____Digoxin.	a.	Coreg®.
____Enalapril.	b.	Xylocaine®.
____Diltiazem.	c.	Lanoxin®.
____Carvedilol.	d.	Cardizem®.
____Metoprolol.	e.	Vasotec®.
____Lidocaine.	f.	Lopressor®.
____Simvastatin	g.	Lopid®
____Gemfibrozil	h.	Zocor®

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 3

1. a (para 3-2)
2. c (para 3-6a)
3. a (para 3-6)
4. b (para 3-11d)
5. b (para 3-11c)
6. c (para 3-11f)
7. c (para 3-4b)
8. d (para 3-11c)
9. d (para 3-9a)
10. a (para 3-12).
11. d. (para 3-12, 3-15(a))
12.

Column A	Column B
c Digoxin. (para 3-7a)	a. Coreg®.
e Enalapril.(para 3-4b,c)	b. Xylocaine®.
d Diltiazem.(para 3-11g)	c. Lanoxin®.
a Carvedilol.(para 3-8a)	d. Cardizem®.
f Metoprolol (para 3-11c)	e. Vasotec®.
b Lidocaine. (para 3-11e)	f. Lopressor®.
h Simvastatin (para 3-15b(1))	g. Lopid®
g Gemfibrozil (para 3-15b(3))	h. Zocor®

End of Lesson 3

LESSON ASSIGNMENT

SUBCOURSE MD0806	Therapeutics III.
LESSON 4	Vasodilatory Drugs**.**
LESSON ASSIGNMENT	Paragraphs 4-1--4-5.
LESSON OBJECTIVES	After completing this lesson you will be able to:

4-1. Given one of the following terms: vasodilator, orthostatic hypotension, angina pectoris, arteriosclerosis, antherosclerosis, or peripheral vascular disease and a group of statements, select the statement that best defines the given term.

4-2. Given the trade or generic name of a vasodilator and a list of trade and/or generic names of drugs, select the trade or generic name that corresponds to the given trade or generic name.

4-3. Given the trade or generic name of a vasodilator and a list of indications, uses, side effects, patient precautionary statements, or dispensing statements, select the indication(s), use(s), side effect(s), patient precautionary statement(s), or dispensing statement for the given drug name.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 4

VASODILATOR DRUGS

Section I. DEFINITIONS

4-1. INTRODUCTION

Visualize a man walking down a hallway. He pauses at the foot of a stairway. From his pocket, he takes a small bottle containing some very small white tablets and he places one of these tablets under his tongue. After waiting a few seconds, he proceeds up the stairs. What was this scene? It was a man preparing his body--especially his heart--for the extra work required for walking up the stairs. This man, suffering from a condition called angina pectoris, used one of the vasodilators that will be discussed in this subcourse lesson. Without this drug, he would be unable to perform many of the energy expending tasks required for everyday life. In this lesson, you will be given the opportunity to broaden your background in some cardiovascular diseases as well as learn more about various vasodilators.

4-2. IMPORTANT TERMS AND THEIR DEFINITIONS

You have already been introduced to some of the terms below in another lesson in this subcourse. Some of the terms below might be new to you. In any event, each term applies to vasodilator agents.

a. **Vasodilator.** A vasodilator is a drug that dilates blood vessels with a resultant increase in blood flow.

b. **Orthostatic Hypotension.** Orthostatic hypotension is a condition characterized by fainting or dizziness because of inadequate blood supply to the brain because the blood has been pooled elsewhere in the body. Vasodilator agents may cause this condition. You may have experienced this condition before. Have you ever arisen quickly from a lying position to find that you are light-headed and dizzy? This is orthostatic hypotension.

c. **Angina Pectoris**. Angina pectoris is a condition manifested by excruciating chest pain sometimes radiating down the left arm. The pain probably arises from ischemia (lack of oxygen) in the heart caused by the increased demand for or decreased supply of oxygen.

d. **Arteriosclerosis**. Arteriosclerosis is characterized by thickening, hardening, and loss of elasticity of the walls of blood vessels.

e. **Atherosclerosis.** Atherosclerosis is a form of arteriosclerosis characterized by localized accumulation of lipids (fats), leading to a narrowing of the arteries and possible occlusion (blockage) of the vessels.

f. **Peripheral Vascular Disease**. Peripheral vascular disease (PVD) is a condition characterized by a narrowing or occlusion of peripheral arterioles leading to limited circulation to the extremities such as toes, fingers, and shoulders. You have probably seen elderly patients who wear extra clothing during hot weather. The cold feeling they have, even in hot weather, is probably due to lack of adequate circulation.

Section II. VASODILATOR DRUGS

4-3. INTRODUCTION

Now that you have some background in some cardiovascular disease, you will review some general categories of vasodilators and some of the specific agents that belong to each group.

4-4. SMOOTH MUSCLE RELAXANT VASODILATORS

Although the agents in this category affect almost all smooth muscle, our concern here is only with their relaxant effect upon the smooth muscle of the coronary vessels as well as peripheral (to the heart) blood vessels.

a. **Amyl Nitrite**. Amyl nitrite is a vasodilator administered only by inhalation. It is rapidly absorbed from the lungs. This product is supplied in perles (like many ammonia inhalants). When a person suffering from angina pectoris feels an attack about to occur, he will crush an amyl nitrite perle and inhale its vapors. The attack of angina pectoris is warded off or aborted in from one to two minutes. Because amyl nitrite perles may explode when stored above normal room temperature, it is very difficult for the patient to carry them in his pocket. This adverse situation normally prohibits their use in the treatment of angina pectoris. The side effects associated with amyl nitrite are usually attributed to the relaxation of all smooth muscle causing vasodilation. Headache and dizziness are very common side effects associated with amyl nitrite. Amyl nitrite does have an additional use, which is the treatment of cyanide poisoning.

b. **Glyceryl Trinitrate (Nitroglycerin).** Glyceryl trinitrate is the most common smooth muscle relaxant vasodilator used in the treatment of acute angina pectoris. This drug is the product described in the introductory remarks of this subcourse lesson when the man placed the small tablet under his tongue. Sublingual nitroglycerin tablets may be used to allow a person who has angina to do extra work or to alleviate an acute angina attack. Nitroglycerin's sublingual onset of action is from 1 to 3 minutes with duration of action of from 9 to 11 minutes. Side effects associated with this drug include headache, dizziness, and orthostatic hypotension. The vasodilating effect of the drug may be so sudden that circulating blood pools in vascular (vessel) beds. This may cause the patient to become unconscious because of a lack of blood to the brain. Falling to the floor in a faint allows the immediate return of that blood flow to the brain and consciousness returns. Besides the sublingual form of nitroglycerin, sustained

release capsules (Nitro-Bid Plateau Caps®) with 5 to 20 milligrams of drug taken daily in divided doses, topical ointments (Nitrol®, Nitro-Bid®), and transdermal patches (Nitro-Dur®) are available. The ointment is applied using special paper every 6 hours. The transdermal system patches are applied to the chest wall each morning and removed after 12 hours. The patches offer the advantage of once daily dosing and less side effects for the patient. Each of these dosage forms is used for the prevention of angina attacks. Nitroglycerin sublingual tablets are volatile. They will lose their potency quickly when they are incorrectly stored. Therefore, the tablets must be dispensed in their original container (light-resistant container). The patient should also be instructed not to remove the tablets from the original glass container (that is, to place the tablets in a fancy pillbox). Federal law requires that all nitroglycerin products should be dispensed in their original containers (that is, glass, light resistant, and not child-resistant packaging). Another problem area with the nitroglycerin prescription is the dose. Normally physicians prescribe them in grains using 1/100 grain, 1/150 grain, or 1/200-grain tablets. You should be able to convert these to micrograms or milligrams. Intravenous nitroglycerin is used in patients that present with unstable angina (persisting chest pain) or possible myocardial infarction. The physician normally orders the nitroglycerin as a drip (mcg/min) and titrates (adjusts) the dose to pain relief.

c. **Isosorbide Dinitrate (Isordil® Sorbitrate®).** Isosorbide dinitrate is thought to be effective in the prophylactic treatment of angina pectoris, as well as the treatment of acute angina attacks. The side effects associated with this drug are headache and dizziness. Isordil® is supplied in many different dosage forms to include sublingual, chewable, compressed, and sustained action tablets and capsules (Tembids®). The sublingual tablets are used in the acute angina attacks in a dose of from 2.5 to 10 milligrams. The usual oral dose is from 15 to 80 milligrams daily in divided doses. These products should be dispensed in their original containers. Isosorbide mononitrate (Ismo®, Imdur®) is another product often prescribed.

NOTE: Tolerance develops to nitrate products. For the agents to maintain effectiveness, the patient must have a “nitrate-free” interval as part of the dosing regimen. Nitroglycerin patches are generally applied in the morning and removed in the evening (12 hours on and 12 hours off). Isosorbide products are administer in the morning, usually at 7am or 8 am, with the second dose after 7 hours later (2 pm to 3 pm). No additional doses are administered so that the patient has a nitrate-free interval.

d. **Hydralazine (Apresoline®) and Minoxidil (Loniten®)**. Hydralazine and Minoxidil are direct acting peripheral vasodilators used in the treatment of hypertension. Hydralazine may be prescribed in combination with an oral nitrate in the treatment of congestive heart failure. The addition of hydralazine further dilates peripheral vessels and decreases workload on the heart.

4-5. AUTONOMIC NERVOUS SYSTEM VASODILATORS

The agent discussed in this paragraph is thought to dilate blood vessels supplying blood to skeletal muscles. Isoxsuprine (Vasodilan®) is sometimes used in the treatment of various conditions causing peripheral vascular disease. Dilating blood vessels to skeletal muscles allows greater blood flow to peripheral areas of the body. Such increased blood flow alleviates some of the symptoms normally associated with peripheral vascular disease (for example: numbness or tingling sensations in the toes and fingers or a feeling of never being warm enough regardless of the atmospheric temperature). The effectiveness of this agent has not been supported by objective studies. The side effects associated with isoxsuprine therapy are severe rash (with some patients), tachycardia, and nausea and vomiting. Vasodilan® is supplied as 10 milligram and 20 milligram tablets. The usual daily dosage is 30 milligrams to 80 milligrams in 4 divided doses.

Continue with Exercises

EXERCISES, LESSON 4

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. A vasodilator is a drug that:

   a. Dilates blood vessels with a resultant increase in blood flow.

   b. Removes deposits of fat and calcium from the inside of vessels in order to increase blood flow.

   c. Causes the heart to beat faster causing an increase in blood flow to the brain and to the peripheral areas.

   d. Counteracts inadequate blood flow to the brain and peripheral areas by causing the arteries and veins to become more elastic.

2. Orthostatic hypotension is a condition characterized by:

   a. Dizziness, fainting, or vertigo caused by a rupture of blood vessels of the brain.

   b. Dizziness or fainting caused by excessive flow of blood to the semicircular canals of the inner ear.

   c. Fainting or dizziness because of inadequate blood supply to the brain.

   d. Fainting or dizziness caused by lack of adequate exercise.

3. Atherosclerosis is best defined as:

    a. A condition characterized by thickening, hardening, and a loss of elasticity of the walls of the blood vessels.

    b. A condition manifested by excruciating chest pain caused by lack of oxygen in the heart.

    c. A form of arteriosclerosis characterized by localized accumulation of fats in the arteries.

    d. A form of angina pectoris in which the vessels of the heart are occluded by fats and carbohydrates.

4. Amyl nitrite is a vasodilator that is used in the treatment of:

    a. Angina pectoris.

    b. Frostbite.

    c. Cyanide poisoning.

    d. a and b.

    e. a and c.

5. Isoxsuprine is used in the treatment of:

    a. Tachycardia.

    b. Various conditions causing peripheral vascular disease.

    c. Orthostatic hypotension.

    d. Irregular heartbeat and muscle tension.

6. What side effects are associated with nitroglycerin?

    a. Irregular heartbeat and tachycardia.

    b. Orthostatic hypertension and sedation.

    c. Acute angina attacks and flushing of the face.

    d. Headache and dizziness.

7. Hydralazine is used in:

   a. The treatment of hypertension and congestive heart failure.

   b. The treatment of night leg cramps and frostbite.

   c. The treatment of atherosclerosis.

   d. The prophylactic treatment of angina pectoris.

8. Which of the following best describes the concept of “nitrate-free” interval associated with the use of nitrates?

   a. Nitrates prescribed day on/day off, to reduce side effects.

   b. Nitrates prescribed 8-12 hours per day, followed by a 12-16 hours drug free interval to decrease tolerance and side effects.

   c. Nitrates prescribed every 6-8 hours and instructed to skip every other dose.

   d. Nitrates prescribed week on/week off, to reduce tolerance and side effects.

9. Match the drug name listed in Column A with its corresponding name listed in Column B.

COLUMN A	COLUMN B
_____ Minoxidil.	a. Sorbitrate®
_____Isosorbide dinitrate.	b. Nitroglycerin.
_____Isoxsuprine.	c. Loniten®.
_____Isosorbide mononitrate.	d. Imdur®.
_____Glyceryl trinitrate.	e. Vasodilan®.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 4

1. a (para 4-2a)

2. c (para 4-2b)

3. c (para 4-2e)

4. e (para 4-4a)

5. b (para 4-5a)

6. d (para 4-4b)

7. a (para 4-4d)

8. b (para 4-4c)

9.

c	Minoxidil.	a.	Sorbitrate®.	(para 4-4d)
a	Isosorbide dinitrate.	b.	Nitroglycerin.	(para 4-4c)
e	Isoxsuprine.	c.	Loniten®.	(para 4-5a)
d	Isosorbide mononitrate.	d.	Imdur®.	(para 4-4c)
b	Glyceryl trinitrate.	e.	Vasodilan®.	(para 4-4b)

End of Lesson 4

LESSON ASSIGNMENT

SUBCOURSE 806 Therapeutics III.

LESSON 5 Drugs Acting on the Hematopoietic System.

LESSON ASSIGNMENT Paragraphs 5-1--5-10.

LESSON OBJECTIVES After completing this lesson you will be able to:

5-1. Given a group of statements, select the statement which best describes hematopoietic drugs.

5-2. Given one of the following terms: coagulant, anticoagulant, hematinic, or growth factors, and a group of statements, select the statement that best defines the given term.

5-3. Given a list of the steps involved in the clotting of blood and a group of sequences of those steps, select the proper sequence of those steps required for clotting of the blood.

5-4. Given the trade or generic name of a drug that acts on the hematopoietic and a list of other trade and generic names, select the trade or generic name that corresponds to the given name.

5-5. Given the trade and/or generic name of a drug that acts on the hematopoietic system and a list of indications, uses, side effects, or precautionary statements, select the indication(s), use(s), side effect(s), or precautionary statement(s) for that drug.

5-6. Given a group of statements, select the statement which should be communicated to each patient to whom an anticoagulant is dispensed.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 5

DRUGS ACTING ON THE HEMATOPOIETIC SYSTEM

Section I. DEFINITIONS

5-1. INTRODUCTION

The word hematopoietic means “blood producing.” Therefore, drugs acting on the hematopoietic system would pertain to drugs that act on the blood producing system of the body. As you might expect, these drugs are potentially dangerous because they can affect blood production in the body.

5-2. DEFINITIONS

a. **Coagulant**. A coagulant is a drug that stimulates the clotting of the blood. Coagulants can be of great aid in an emergency in which the patient may be losing a large volume of blood.

b. **Anticoagulant**. An anticoagulant is a drug that prevents the clotting of the blood. Anticoagulants are used in various types of surgery as well as in everyday use in order to control blood clots.

c. **Hematinic**. A hematinic is a drug that stimulates the formation of red blood cells. Hematinics are used in the treatment of anemias.

d. **Stimulating Factors.** A stimulating factor is an agent that stimulates the formation of specific blood cells (red blood cells, white blood cells, or platelets).

Section II. COAGULANTS

5-3. REVIEW OF THE CLOTTING PROCESS

The area of blood clotting was discussed in paragraphs 2-7 and 2-8 of this subcourse. The actual clotting of blood involves several steps. Each step is essential to clotting. Refer to figure 5-1.

a. **STEP 1**. The blood platelets release a substance that is known as thromboplastin.

b. **STEP 2**. Thromboplastin reacts with calcium and another substance, prothrombin, to form thrombin. Vitamin K is necessary for the proper formation of prothrombin.

c. **STEP 3**. The thrombin formed acts as an enzyme to convert fibrinogen to fibrin threads that eventually form the blood clot.

d. **STEP 4.** Clot breakdown: Plasminogen binds to fibrin as the clot forms. In response to thrombin formation and venous stasis (clot), plasminogen activators convert plasminogen to plasmin. Plasmin digests fibrin and dissolves the clot.

NOTE: For a more in-depth discussion of blood clotting you should locate and read a physiology text that is appropriate to your level of understanding.

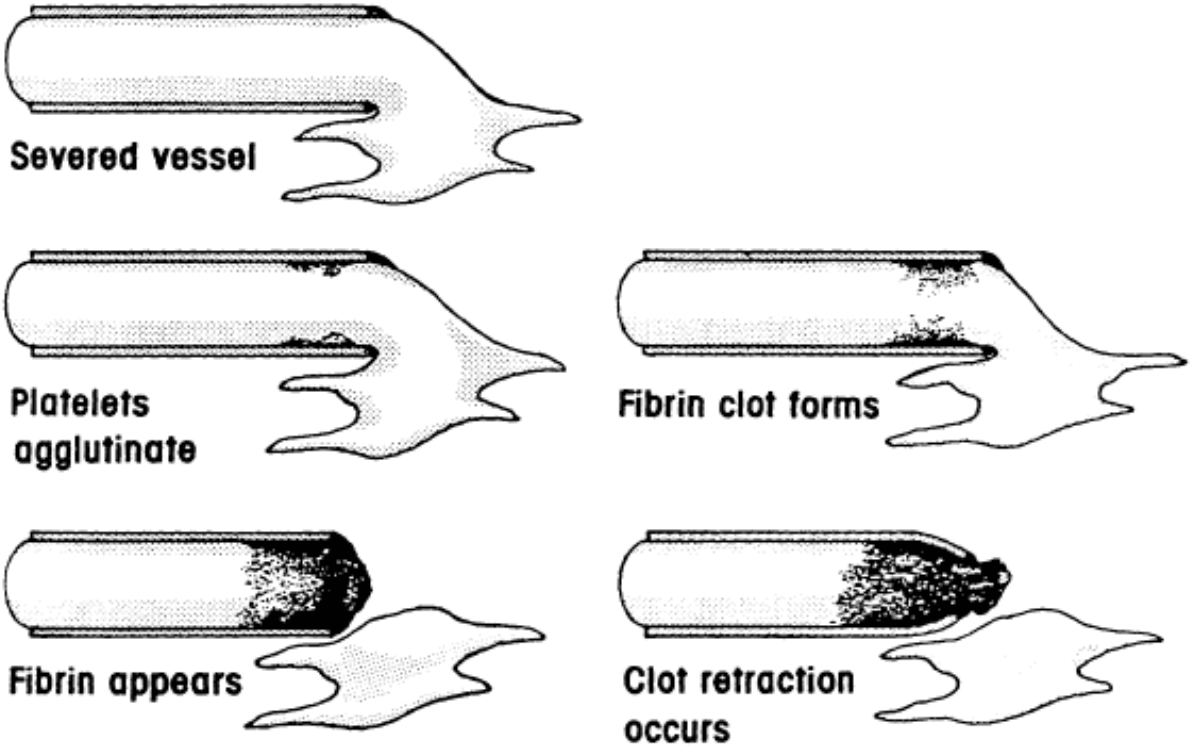


Figure 5-1. The blood clotting process.

5-4. COAGULANTS (PROMOTING CLOT FORMATION)

There are several drugs that affect the clotting process at different stages to promote coagulation. Vitamin K derivatives and coagulation factors work by enhancing the formation or increasing the amount of circulating clotting factors and promoting the coagulation process (steps 2 and 3 of paragraph 5-3). Drugs that inhibit plasminogen or plasmin result in coagulation by preventing the breakdown of clots (step 4 of paragraph 5-3).

a. **Phytonadione (Mephyton®, Aqua-Mephyton®, Vitamin K_1)**. Phytonadione or vitamin K is the most commonly prescribed coagulant and antidote for warfarin overdose. As a coagulant, the usual dose is 0.5 to 1.0 milligram given intramuscularly (IM) to infants at birth to prevent infant hemorrhagic disease. Infants are administered this medication because at birth they lack the normal intestinal flora required to produce

enough Vitamin K to play its role in blood clotting. When phytonadione is used for its anticoagulant effects, the dosage is based on the level of warfarin anticoagulation in the patient. This level of anticoagulation is determined by blood sample and expressed as the International Normalized Ratio (INR) by the laboratory. Doses may be as small as 0.5 to 1 mg (oral) and up to 10 mg administered subcutaneously. The initial effects of vitamin K take up to 6 hours with maximum effects in two to three days. If a patient is actively bleeding, the coagulant of choice may be fresh frozen plasma or a blood transfusion. Side effects associated with this agent include "flushing" sensations and peculiar sensations of taste. The injectable form of this agent is used only on an inpatient basis (that, in the hospital or emergency room), and it should be remembered that it should only be administered subcutaneously--severe reactions (including death) have been reported when the product was given intravenously (IV). Phytonadione will not counteract the anticoagulant action of heparin.

b. **Vitamin K_3, Menadione.** Menadione is another coagulant prescribed in patients who have bleeding problems. The only side effect of real concern with menadione is hepatomegaly. Hepatomegaly is a condition in which the liver becomes enlarged because of an excess of fat soluble vitamins stored in the lipid tissue. This agent is commonly supplied in tablet form.

c. **Menadiol (Synkayvite®)**. Menadiol (observe its similarity to menadione) is a synthetic Vitamin K_3. Menadiol is also used as a coagulant available in a tablet and injectable form.

d. **Specific Clotting Factors.** In patients who have an acquired or hereditary clotting factor deficiency, specific clotting factors are available. Factor VIII and Factor IX are available as concentrates and are often stocked within the pharmacy. These agents are available for minor procedures or surgery in select patients with deficiencies.

e. **Desmopressin Acetate (DDAVP®).** Desmopressin is a synthetic analog of vasopressin, the naturally occurring human antidiuretic hormone. It has the unique activity of producing a dose-related increase in circulating Factor VIII and von Willdebrand's factor levels. Both of these factors are essential to normal human coagulation. This agent is used in individuals with Hemophilia A (lacking factor VIII) or von Willdebrand's disease. Desmopressin will maintain homeostasis in these patients during surgery and post-operatively. Desmopressin may also be prescribed for uncontrolled bleeding related to surgery in patients without a coagulation dysfunction.

f. **Aminocaproic Acid (Amicar®).** Aminocaproic acid is an agent that inhibits fibrinolysis (clot breakdown) by inhibiting plasminogen activators. Consequently, it stabilizes clots in excessive bleeding. Aminocaproic acid is given either intravenously or orally. Individuals with bleeding dysfunction (hemophilia) may take this product 12 to 24 hours prior to a dental procedure or surgery. It is often prescribed with desmopressin.

g. **Tranexamic Acid (Cyklokapron®) and Aprotinin (Trasylol®).** Tranexamic acid is a competitive inhibitor of plasminogen activation. Its action is similar to aminocaproic acid, but approximately 10 times more potent. It is used in hemophiliacs undergoing invasive procedures. Apotinin is a natural protease inhibitor that inhibits plasmin. It is used prophylactically in patients undergoing coronary artery bypass surgery to prevent peri-operative blood loss.

NOTE: The administration of blood products (whole blood, fresh frozen plasma, or cryoprecipitate) may be used in place of any or all of the above agents to correct excess bleeding. They are often the fastest means of correcting excess anticoagulation. Although each of the drugs discussed above has side effects, the risk/benefit of a transfusion must be weighed in each patient.

Section III. ANTICOAGULANTS

5-5. INTRODUCTION

a. Just as there are conditions of excess bleeding (anticoagulation), so are there conditions in which excess clotting (coagulation) may be detrimental to the patient. The major components that promote excess clot formation are listed below.

(1) Venous stasis. Venous stasis (altered or decrease blood flow to the deep veins) occurs with impaired mobility (traumatic injury, obesity, etc.).

(2) Vascular injury. Vascular injury occurs as the result of mechanical or chemical trauma causing an inflammation of the vessel.

(3) Hypercoagulability. Hypercoagulability results from a deficiency of natural anticoagulants (antithrombin III, protein C, protein S) or a specific disease state (such as cancer).

b. Anticoagulants are essential to correcting the propensity to clot. However, they are a potentially dangerous class of drugs. One reason for their dangerous status is that anticoagulants interact with a variety of medications (over the counter and legend). Second, there is always a risk of uncontrolled bleeding when you inhibit a process that promotes clotting. One of the most important interactions to remember is the combination of anticoagulants with other drugs--especially salicylates (aspirin) or non-steroidal anti-inflammatory drugs (ibuprofen, naproxen). These products can potentiate the effects of the anticoagulants by inhibiting platelet aggregation which is the first line of defense to stop bleeding.

5-6. IMPORTANT WARNING ASSOCIATED WITH THE ANTICOAGULANTS

There is one warning common to all anticoagulants. When you dispense an anticoagulant to a patient you should tell the person that they should not take any other medication--over the counter or legend--without first consulting the physician who

prescribed the anticoagulant. Emphasize that over-the-counter products such as aspirin and ibuprofen are also classified as medications.

5-7. ANTICOAGULANT AGENTS

a. **Anti-platelet Agents.** Anti-platelet agents are used to prevent a clot from forming (step I) or prevent the clot from getting larger and occluding the entire vessel. All patients must be warned of the increased risk of bleeding when taking these drugs.

(1) Aspirin**.** Aspirin is the most widely used anti-platelet drug. It inhibits platelet aggregation for the life of the platelet (7 to 10 days). Because of this effect, aspirin is prescribed in the setting of acute myocardial infarction and prophylactically to prevent reinfarction. Always ask the patient if he has an allergy to aspirin.

(2) Clopidogrel (Plavix®) and Ticlopidine (Ticlid®)**.** Clopidogrel and ticlopidine work by inhibiting platelet aggregation. They are often prescribed for patients that have an aspirin allergy or are intolerant of aspirin (usually stomach upset). Both agents may be used in patients with atherosclerotic disease to prevent heart attacks, prevent stokes, and prevent coronary artery closure in patient undergoing angioplasty. Ticlopidine is administered twice daily and is associated with a risk of decreased white blood cells (neutropenia). Clopidogrel is administered once daily and has a much lower risk of neutropenia. Both agents can cause a rash.

(3) Dipyridomole (Persantine®)**.** Dipyridomole works by inhibiting platelets from adhering to the injured cell wall. Although not used extensively, it may be prescribed in combination with other anticoagulants. The combination product of dipyridomole and aspirin is called Aggrenox®**.**

(4) Abciximab (ReoPro®), Tirofiban (Aggrastat®), and Eptifibatide (Integrelin®)**.** These agents are known as glycoprotein IIb/IIIa inhibitors. The GP IIb/IIIa receptor is the major receptor on the platelet responsible for platelets adhering to each other and forming the initial clot. These drugs are administered intravenously in patients with acute coronary syndromes (unstable angina) or in patients undergoing angioplasty with or without stent placement in the cardiac catheterization lab. The agents prevent clots from forming the coronary arteries of the heart. The agents are not interchangeable and differ in their respective half-lives and infusion schedules. The major side effect is thrombocytopenia (low platelet count), often requiring platelets be checking during infusion in patients.

b. **Heparin Products.** Heparin is used to prevent the clotting of blood in the patient and in laboratory samples by inhibiting certain clotting factors (thrombin/Factor IIa and Factor Xa). Like anti-platelet drugs, heparin will not dissolve a clot, but prevents it from getting larger. The dosage of this agent is based upon the needs of the patient (prophylactic vs. treatment doses). It may be administered subcutaneously or intravenous (IV push or IV continuous infusion). The major side effect associated with heparin is possible hemorrhage. Protamine sulfate is used to treat heparin overdose.

Although protamine sulfate is also an anticoagulant, it counteracts the effects of heparin by binding with the heparin. The net result is removing the effects of the heparin. The primary side effects associated with protamine sulfate are temporary hypotension, bradycardia, and dyspnea.

(1) Heparin sodium, heparin calcium. Commerical heparin (unfractionated heparin) comes from beef lung or pork intestinal mucosa. It is dosed in "units" and measured in the lab by the partial thromboplastin time (PTT). Although some heparin is administered in a "fixed dose" for prophylaxis against clots, it is more often administered in a "wt-based" fashion for prophylaxis and treatment of clots. Therapeutic dose goals are 1.2 to 1.5 times the PTT control. Doses, especially for continuous infusion, are adjusted to meet this goal. Heparin may be administered in a very small fixed dose (10 to 100 units) to clear intravenous ports in patients with long term IV lines. This dose is called a "heparin flush". The absorption of subcutaneous heparin is unpredictable.

(2) Enoxaparin (Lovenox®), Dalteparin (Fragmin®). Enoxaparin and dalteparin are two of several "low molecular weight heparins (LMWH)" (fractionated heparin). They differ from unfractionated heparin by having more predictable subcutaneous absorption, a longer duration of action, and primarily inhibit only one clotting factor (Factor Xa). Either agent may be administered once or twice daily (SC) usually for 7 to 10 days. The primary use for these agents is in the prevention and treatment of deep vein thrombosis (leg clots) and pulmonary embolus (lung clots). The side effects are the same as with unfractionated heparin; however, they offer distinct advantages in that the patient can self-administer these agents (discharged from the hospital sooner). They do not require monitoring of the PTT and are just as effective as standard heparin. The major disadvantages are pain at the injection site and high cost.

c. **Coumarin Products**.

(1) General. Coumarin products inhibit coagulation by interfering with the incorporation of vitamin K into vitamin-K dependent clotting factors (Factors II, VII, IX, and X). Their initial and maximum effect is based on the half-lives of each of these factors. For example, Factor VII has a half-life of 6 hours, so the effect of coumarin on this factor will increase the bleeding to a certain degree within 6 hours. However, Factor II and X exhibit half lives of 48 to 72 hours, so the maximum effect of coumarin is not seen until 3 days after initiation or dose change. It does not matter whether the drug is given orally or intravenously; it take the same amount of time to reach the maximum effect (essentially, you cannot load a patient on coumarin agents). Coumarin products do not dissolve clots, but prevent clots from forming (prophylaxis) and getting larger. The degree of anticoagulation is measured by a blood sample and expressed at the prothrombin time (PT) or the International Normalized Ratio (INR). The INR is the international standard. The therapeutic INR is generally between 2 and 3.5, which correlates with a 30 to 50 percent inhibition of vitamin K dependent clotting factors. Ideally, the patient should have his INR checked every 4 to 6 weeks while on this medication.

(2) Warfarin sodium (Coumadin®). Warfarin sodium is one of the most commonly used anticoagulants (coumarins). It is used to prevent the extension of blood clots in phlebitis or deep vein thrombosis and as a prophylactic agent in patients that have mechanical heart valves (life-long therapy). The main side effect associated with the use of warfarin sodium is hemorrhaging. This product is available in both oral and injectable forms.

CAUTION: Warfarin sodium has over 50 documented drug-drug interactions. You must research this drug carefully against the patient profile before dispensing.

d. **"Clot Busters."** As discussed above, aspirin, heparin, or warfarin can be administered to prevent clots or stop clots from getting bigger. However, none of these drugs can dissolve a clot that is already established. In many cases, we cannot wait for the body to reabsorb these clots back into the lining of the vessel (4 to 6 months); the clot needs to be dissolved immediately. This is true in the case of patients having heart attacks and strokes. "Clot busters" do just that. By acting as tissue plasminogen activator and converting plasminogen to plasmin or mimicking fibrinolytic enzymes, they break down the clot. These agents are always administered intravenously and require close observation for bleeding in the patient. They are most effective when administered as close to onset of symptoms as possible (ideally within 3 to 6 hours).

(1) Streptokinase (Streptase®) Urokinase ((Abbokinase®)**.** Streptokinase and urokinase were some of the first clot busters developed and act as fibrinolytic enzymes. Streptokinase comes from streptococcus species, so patients with strept antibodies may have an allergic reaction to this agent. Urokinase comes from human kidney cells, so the incidence of side effects is less. Both agents are administered via continuous IV infusion (12 to 24 hours) and are rarely used with the advent of recombinant products.

(2) Alteplase (Activase®)**.** Alteplase, also known as tPA (tissue plasminogen activator), was the first recombinant product developed. It offers the advantage of short infusion time (1 hour) and is more effective than streptokinase. It is used for heart attacks (within 4 to 6 hours of symptoms) and stokes (within 3 hours of symptoms). Alteplase (2 mg) is also used to dissolve clots in IV lines. Reteplase (Retavase®) and anistreplase (Eminase®) are other clot busters.

Section IV. HEMATINICS

5-8. INTRODUCTION

Hematinics are drugs used to stimulate the formation of red blood cells. These agents are used primarily in the treatment of certain types of anemias. Some of these preparations are routinely given to women during pregnancy.

5-9. HEMATINIC AGENTS

a. **Ferrous Gluconate (Fergon®) Ferrous Sulfate (Feosol®).** Ferrous gluconate and ferrous sulfate are used to treat iron deficiency anemia. The usual dosage given is one to four times daily. Side effects associated with these agents include gastrointestinal upset, constipation, and black stools. Warn the patient about these possible side effects.

b. **Iron Dextran (InFed®).** This drug is also used to treat iron deficiency anemia. Side effects associated with this agent include gastrointestinal upset, constipation, and black stools. Extreme caution should be observed with this product because it is administered parenterally and some patients have demonstrated an anaphylactic type reaction to the drug. This product is used on an inpatient basic and is administered by injection. Iron dextran should not be administered concurrently with oral iron preparation because the side effects mentioned above will be potentiated.

c. **Cyanocobalamin, Vitamin B_{12} (Rubesol-1000®).** Cyanocobalamin is used in the treatment of pernicious anemia. Pernicious anemia is a condition characterized by a progressive decrease in the number and an increase in the size of red blood cells. Patients who have this condition are usually very weak and have various gastro-intestinal disturbances. This condition results from a lack of Vitamin B_{12}. This occurs because of the lack of intrinsic factor, an element that is needed in the intestine in order to effectively absorb Vitamin B_{12}. Thus, cyanocobalamin is used to replace the Vitamin B_{12} that was not absorbed. Cyanocobalamin should be protected from light. It is available in injectable or tablet form.

d. **Folic Acid (Folate®).** Folic acid is used in combination with other drugs to treat pernicious anemia because it causes an increase in the number of red blood cells. If the drug is administered alone to treat pernicious anemia, it will mask the symptoms of that condition. This is potentially dangerous because if the symptoms are masked, the condition might flourish and cause irreversible neurologic damage. Folic acid is available in both tablet and injectable dosage forms.

e. **Erythropoetin; EPO; Epoten alfa (Epogen®, Procrit®).** Erythropoetin is a protein naturally produced in the kidney that stimulates red blood cell production. It is administered in a variety of chronic anemia states (cancer, renal failure, dialysis, and HIV infection). It may also be used prophylactically to reduce the need for a blood transfusion in patients scheduled for major surgery. The major side effect of erythropoetin is hypertension, especially if the hematocrit rises above 36 percent. Erythropoetin is administered subcutaneously one to three times weekly. Single dose vials MUST be disposed of immediately after use. Multi-dose vials are discarded 21 days after initial entry. Erythropoetin requires refrigeration.

Section V. STIMULATING FACTORS

5-10. INTRODUCTION

Stimulating factors are naturally occurring substances that promote the proliferation of blood components. Similar to the effects of erythropoetin stimulating the production of red blood cells, the stimulating factors discussed below affect the production of white blood cells and platelets.

a. **Granulocyte Colony Stimulating Factor; G-CSF; Filgrastim (Neupogen®).** Filgrastim stimulates the growth of white blood cells, specifically the granulocytes (neutrophils). It is used in the treatment of neutropenia (low neutrophils) from chemotherapy or bone marrow transplant patients. The most common complaints associated with use are nausea, vomiting and joint aches. Filgrastim is administered subcutaneously 5 to 10 mcg/kg/day until neutrophil counts rise to normal. Filgrastim is available as an injection without preservative. Filgrastim requires refrigeration.

b. **Granulocyte Macrophage Colony Stimulating Factor; GM-CSF; Sargramostim (Leukine®).** Sargramostim is used to stimulate the proliferation of granulocytes and macrophages in patients with leukemia and/or undergoing bone marrow transplant. This agent is administered 250 mcg/m^2/day via IV infusion over 2 to 4 hours until neutrophil recovery. The side effects are similar to filgrastim. Sargramostim must be refrigerated.

Continue with Exercises

EXERCISES, LESSON 5

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. Which of the following statements best describes hematopoietic system drugs?

   a. Drugs that produce pernicious anemia or mask its effects on the body.

   b. Drugs that clot the blood.

   c. Drugs that act on the blood producing system of the body.

   d. Drugs that decrease the clotting capability of the blood.

2. Hematinic drugs stimulate the:

   a. Formation of red blood cells.

   b. Clotting of the blood.

   c. Production of hematin in the body.

   d. Mechanism responsible for preventing the clotting of the blood.

3. Immediately below are the three steps involved in blood clotting. Select the sequence of steps that reflect the proper sequence of steps required for blood clotting.

    I. Thromboplastin reacts with calcium and prothrombin to form thrombin. Vitamin K is necessary for the proper formation of prothrombin.

    II. The thrombin formed acted acts as an enzyme to convert fibrinogen to fibrin threads that eventually form the blood clot.

    III. The blood platelets release a substance which is know as thromboplastin.

    a. II, I, and III.

    b. II, III, and I.

    c. III, I, and II.

4. Heparin sodium is used to:

    a. Stimulate the formation of red blood cells.

    b. Stimulate the clotting of the blood in people with clotting difficulties.

    c. Prevent Vitamin K from being formed and absorbed in the body.

    d. Prevent the clotting of blood in the patient and in Laboratory examples.

5. What side effect is associated with ferrous gluconate?

    a. Pernicious anemia.

    b. Black stools.

    c. Phlebitis.

    d. Hepatomegaly.

6. What side effect is associated with enoxaprin?

   a. Black stools.

   b. Phelebitis.

   c. Pernicious anemia.

   d. Hemorrhaging.

7. All of the following classes of drugs are used for anticoagulation EXCEPT:

   a. Clot busters such as alteplase.

   b. Anti-platelets such as aspirin.

   c. Vitamin K derivatives such as phytonadione.

   d. Heparin derivatives such as dalteparin.

8. Folic acid can mask the symptoms of _____ if it is administered alone.

   a. Pernicious anemia.

   b. Iron deficiency anemia.

   c. Hepatomegaly.

   d. Phlebitis.

9, Clot busters are agents used to:

   a. Prevent platelets from adhering to each other.

   b. Block certain clotting factors to prevent blood from clotting.

   c. Stimulate the production of certain blood components.

   d. Dissolve clots that have already formed.

10. Match the drug name in Column A with its trade name in Column B.

	COLUMN A		COLUMN B
_	Ferrous gluconate.	a.	Aqua-Mephyton®.
__	Enoxaprin.	b.	ReoPro®.
__	Iron dextran.	c.	DDAVP®.
__	Phytonadione.	d.	Activase®.
__	Warfarin sodium.	e.	Fergon®.
__	Desmopressin acetate.	f.	Neupogen®.
__	Abciximab.	g.	InFed®.
__	Clopidogrel.	h.	Lovenox®.
__	Aprotinin.	i.	Procrit®.
__	Erythropoetin.	j.	Coumadin®.
__	Alteplase.	k.	Trasylol®.
__	Filgrastim.	l.	Plavix®.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 5

1. c (para 5-l)

2. a (para 5-2c)

3. c (para 5-3)

4. d (para 5-7a)

5. b (para 5-9a)

6. d (para 5-7c)

7. c. (para 5-4)

8. a (para 5-9e)

9. d (para 5-7d)

10.

e	Ferrous gluconate. (para 5-9a)	a. Aqua-Mephyton®.
h	Enoxaprin. (para 5-7b(2))	b. ReoPro®
g	Iron Dextran. (para 5-9b)	c. DDAVP®.
a	Phytonadione. (para 5-4a)	d. Activase®.
j	Warfarin sodium. (para 5-7c(2))	e. Fergon®.
c	Desmopressin acetate (para 5-4e)	f. Neupogen®
b	Abciximab (para 5-7a(4))	g. InFed®.
l	Clopidogrel (para 5-7a(2))	h. Lovenox®
k	Aprotinin (para 5-4g)	i. Procrit®
i	Erythropoetin (para 5-9e)	j. Coumadin®.
d	Alteplase (para 5-7d(2))	k. Trasylol®
f	Filgrastim (para 5-10a)	l. Plavix®

End of Lesson 5

LESSON ASSIGNMENT

SUBCOURSE MD0806 Therapeutics III.

LESSON 6 The Human Urogenital Systems.

LESSON ASSIGNMENT Paragraphs 6-1--6-20.

LESSON OBJECTIVES After completing this lesson you will be able to:

6-1. Given a group of components, select the two components of the human urogenital system.

6-2. Given a group of functions, select the specialized function of the urinary system.

6-3. Given a group of components, select the major components of the human urinary system.

6-4. Given a drawing of the human urinary system and a group of names of the major components of the urinary system, match the name of each major component with its location on the drawing

6-5. From a group of names of structures, select the name of the functional unit of the human kidney.

6-6. From a list of functions, select the functions(s) of the nephron.

6-7. Given a drawing of a nephron and a list of the names of the parts of a nephron, match the name of each part with its location on the drawing.

6-8. Given the name of one of the parts of the nephron and a group of statements, select the statement that best describes the role of the part in the production of urine.

6-9. Given the name of one of the hormones involved in the formation of urine and a group of statements, select the statement that best describes the role of that hormone in the formation of urine.

6-10. Given the name of a part of the urinary system and a group of statements, select the statement that best describes that part of the urinary system.

6-11. Given the name of a urinary tract disorder and a group of statements, select the statement that best describes the disorder.

6-12. From a list of organs, select the primary sex organ in the human female.

6-13. Given the name of a secondary sex organ in the human female and a group of statements, select the statement that best describes the secondary sex organ.

6-14. Given a list of organs, select the primary sex organ in the human male.

6-15. From a group of statements, select the function(s) of the testis.

6-16. Given the name of a secondary sex organ in the human male and a group of statements, select the statement that best describes the secondary sex organ.

SUGGESTION

After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 6

THE HUMAN UROGENTIAL SYSTEMS

Section I. OVERVIEW OF THE UROGENITAL SYSTEMS

6-1. INTRODUCTION

The human urogenital systems are made up of the urinary organs, which produce the fluid called urine, and the genital or reproductive organs, organs of male and female humans, which together can produce a new human being.

6-2. DISCUSSION OF LESSON CONTENT

This lesson will focus on the human urinary and reproductive systems. The urinary system will be discussed first.

Section II. THE HUMAN URINARY SYSTEM

6-3. INTRODUCTION

The urinary system is one of the major systems of your body. When something goes wrong with this system, medical assistance must quickly be obtained. An understanding of the anatomy and physiology of the urinary system will help you as you study such drug categories as diuretics (those drugs which increase urine output).

6-4. THE HUMAN URINARY SYSTEM

a. **Proteins.** Proteins are one of the basic foodstuffs that humans consume. When the body uses proteins, residue or waste products can be poisonous (toxic) if allowed to accumulate in large amounts. The urinary system of the human body is specialized to remove these nitrogenous waste products from the circulating blood.

b. **Major Parts.** See figure 6-1 for the major parts of the human urinary system. This system includes two kidneys, two ureters (one connecting each kidney to the urinary bladder), the urinary bladder, and the urethra.

6-5. THE KIDNEY

a. **General.**

(1) The kidneys have the same shape and color as kidney beans, but are about 8-10 cm (3”-3 1/2”) in length.

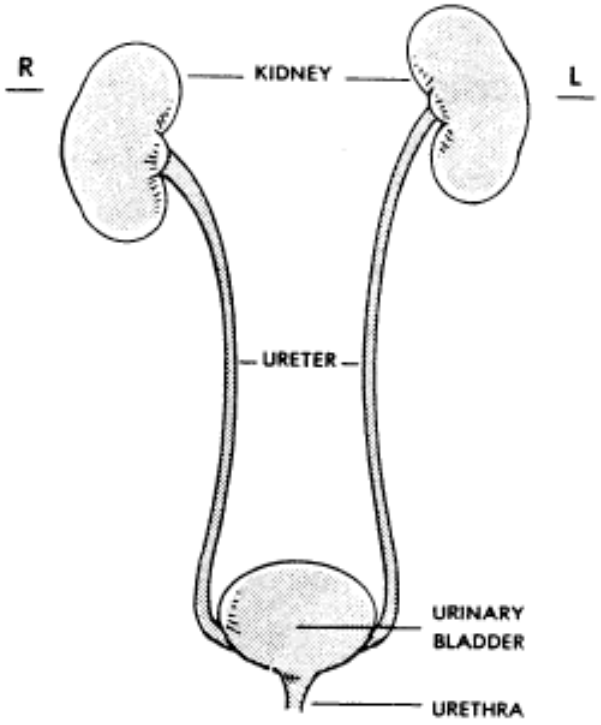


Figure 6-1. The human urinary system.

(2) Each kidney has a fibrous capsule. On the concave, medial side of each kidney, there is a notch called the hilus. Through the hilus, pass the ureter and the NAVL (nerve, artery, vein, and lymphatic), which service the kidney.

(3) Each kidney is attached to the posterior wall of the abdominal cavity, just above the waistline level. Each is held in place by special fascia and fat.

b. **Gross Internal Structure.** If we compare the structure of the kidney with that of a cantaloupe (muskmelon), the renal cortex would correspond to the hard rind, the renal medulla would correspond with the edible flesh of the melon, while the renal sinus would correspond to the hollow center (after the seeds have been removed. The medulla consists of pyramids with their bases at the cortex and forming peaks, papillae, which empty into the sinus. See figure 6-2 for a section of the kidney showing the inner structure.

PAPILLA = pimple, nipple

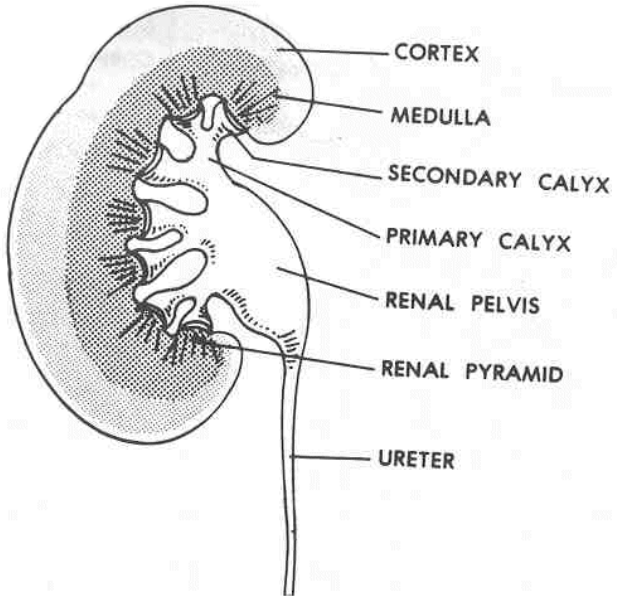


Figure 6-2. A section of a human kidney.

c. **The Nephron.** Nephrons are the functional units of the human kidney. Their primary function is to remove the wastes of protein usage from the blood. In addition, they serve to conserve water and other materials for continued use by the body. The result of nephron function is more or less concentrated fluid called urine. The kidneys contain great numbers of nephrons, about a million for each kidney. The main subdivisions of a nephron are the renal corpuscle and a tubular system. See figure 6-3 for an illustration of a nephron.

(1) Renal corpuscle. The renal corpuscle has a hollow double walled sac called the renal capsule ("Bowman's capsule"). Leading into the capsule is a very small artery called the afferent arteriole. Within the capsule, this artery becomes a mass of capillaries known as the glomerulus. An efferent arteriole drains the blood away from the capsule. The capsule and the glomerulus together are known as the renal corpuscle.

(2) Tubules. Each renal capsule is drained by a renal tubule. The first part of this tubule runs quite a distance in a coiled formation and is called the proximal convoluted tubule. A long loop, the renal loop (of Henle) extends down into the medulla with two straight parts and a sharp bend at the bottom. As the tube returns to the cortex layer, it becomes coiled once more and here is known as the distal convoluted tubule.

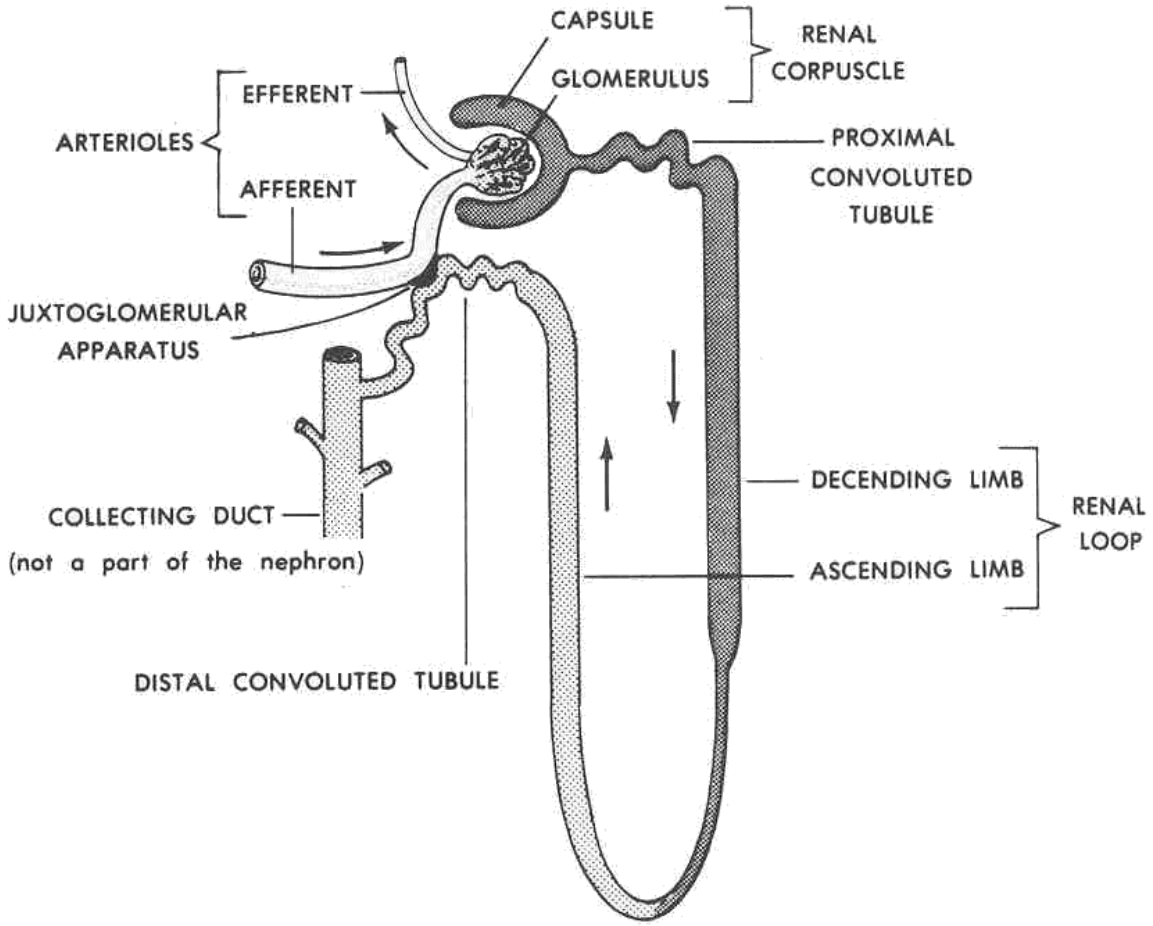


Figure 6-3. A “typical” nephron.

(3) Filtration/reabsorption. Except for the blood cells and the larger proteins, the fluid portion of the blood passes through the walls of the glomerulus into the cavity between the two layers of the renal capsule. This fluid is called the glomerular filtrate. By a process of taking back (resorption), the majority of the fluid is removed from the tubules and the concentrated fluid is called urine.

d. **The Collecting Tubule.** The distal convoluted tubules of several nephrons empty into a collecting tubule. The urine is then passed from the collecting tubule at the papilla of the medullary pyramid. Several collecting tubules are present in each pyramid**.**

e. **Renal Pelvis.** The renal pelvis is a hollow sac within the sinus of the kidney. Urine from the pyramids collects into the funnel-shaped renal pelvis. The ureter then drains the urine from the renal pelvis.

6-6. HORMONES INVOLVED IN THE FORMATION OF URINE

There are two main hormones involved in the formation of urine. These hormones are the antidiuretic hormone (ADH), and aldosterone.

a. **Antidiuretic Hormone.** The antidiuretic hormone is a hormone secreted by the pituitary gland. It acts on the distal and collecting tubules to increase water reabsorption. Since more water is reabsorbed, the urine becomes more concentrated.

b. **Aldosterone.** The aldosterone is secreted by adrenal cortex, that is situated above each kidney. Aldosterone increases sodium reabsorption in the distal tubules and collecting ducts. This leads to an increase in sodium reabsorption and of concentration of the urine.

6-7. URETERS

The ureters are tubes that connect the kidneys to the urinary bladder. The smooth muscle walls of the ureters produce a peristalsis (wave-like movement) that moves the urine along drop by drop.

6-8. URINARY BLADDER

a. The urinary bladder is a muscular organ for storing the urine. Near the inferior posterior corners of the urinary bladder are openings where the ureters empty into the bladder. Also at the inferior aspect of the urinary bladder is the exit, the beginning of the urethra. The triangular area, between the openings of the ureters and the urethra, is called the trigone, or base of the urinary bladder.

b. The urinary bladder wall is stretchable to accommodate varying volumes of urine.

c. Nerve endings called stretch receptors are found in the wall of the urinary bladder. Usually, the pressure within the urinary bladder is low. However, as the volume of the enclosed urine approaches the bladder's capacity, stretching of the wall stimulates the stretch receptors. The cycle of events controlling urination (voiding or emptying of the urinary bladder) is known as the voiding reflex.

6-9. URETHRA

The urethra is a tube that conducts the urine from the urinary bladder to the outside of the body. It begins at the anterior base of the urinary bladder.

a. **Urethral Sphincters**. The urethral sphincters are circular muscle masses that control the passage of the urine through the urethra. There are two urethral sphincters: an internal urethral sphincter and an external urethral sphincter.

(1) The internal urethral sphincter is located in the floor of the urinary bladder. It is made of smooth muscle tissue. Nerves of the autonomic nervous system control it.

(2) The external urethral sphincter is inferior around the urethra in the area of the pelvic floor. It is made up of striated muscle tissue. It is controlled by the peripheral nervous system.

b. **Male-Female Differences**. The female urethra is short and direct. The male urethra is much longer and has two curvatures. Whereas the female urethra serves only a urinary function, the male urethra serves both the urinary and reproductive functions.

6-10. URINARY TRACT DISORDERS

Several disorders can affect the urinary system. Some of these disorders can present serious problems.

a. **Uremia.** Uremia, or as it is frequently called, toxemia, is a condition in which there is a build-up of toxic substances in the blood. These accumulated waste products are in the blood because of kidney failure. This condition can occur during pregnancy, since many pregnant women have fluid retention.

b. **Glomerulonephritis**. Glomerulonephritis is an inflammation of the nephrons--mainly centered in the glomerulus. This condition is due to toxic material produced by bacteria.

c. **Pyelonephritis.** Pyelonephritis is another condition caused by bacteria. Pyelonephritis is an inflammation of the kidney and pelvis area of the kidney.

d. **Edema**. Edema is a build-up of fluids in the tissues. It is found in a variety of conditions (that is, pregnancy, congestive heart failure, and renal disease).

e. **Diabetes Insipidus**. Diabetes insipidus is an increased urine output due to a low production of the antidiuretic hormone. As previously mentioned, the antidiuretic hormone increases the reabsorption of water. A lack of the antidiuretic hormone thus prevents water from being reabsorbed and leads to increased urine output.

f. **Cystitis.** Cystitis is an inflammation of the urinary bladder, which may spread to the kidneys.

Section III. INTRODUCTION TO HUMAN GENITAL (REPRODUCTIVE) SYSTEMS

6-11. SEXUAL DIMORPHISM

The human male and human female each has a system of organs specifically designed for the production of new humans. These systems are known as reproductive or genital systems. Since there are different systems for males and females, the genital systems are an example of sexual dimorphism.

MORPH = form, shape
D1 = two
SEXUAL = according to sex (gender)
SEXUAL DIMORPHISM = having two different forms according to sex

6-12. ADVANTAGES OF DOUBLE PARENTING

The existence of two parents for each child means that genetic materials are recombined to produce a new type. This new type may be an improvement over previous generations.

6-13. MAJOR COMPONENT CATEGORIES OF THE GENTIAL SYSTEMS

Components of the genital systems may be considered in the following categories:

a. **Primary Sex Organs (Gonads)**. Primary sex organs produce sex cells (gametes). A male gamete and a female gamete may be united to form the one-cell beginning of an embryo (the process of fertilization). Primary sex organs also produce sex hormones.

b. **Secondary Sex Organs**. Secondary sex organs care for the product of the primary sex organ.

c. **Secondary Sexual Characteristics**. Secondary sexual characteristics are those traits that tend to make males and females more attractive to each other. Secondary sexual characteristics help to ensure mating. These characteristics first appear during puberty (10-15 years of age).

Section IV. THE HUMAN FEMALE GENITAL (REPRODUCTIVE) SYSTEM

6-14. PRIMARY SEX ORGANS (OVARIES)

The primary sex organ in the human female is the ovary. (See figure 6-4 for an illustration of the female genital system.) The ovaries are located to the sides of the upper end of the uterus. They are anchored to the posterior surface of the broad ligaments. (The broad ligaments are sheets or folds of peritoneum inclosing the uterus and uterine tubes and extending to the sides of the pelvis.)

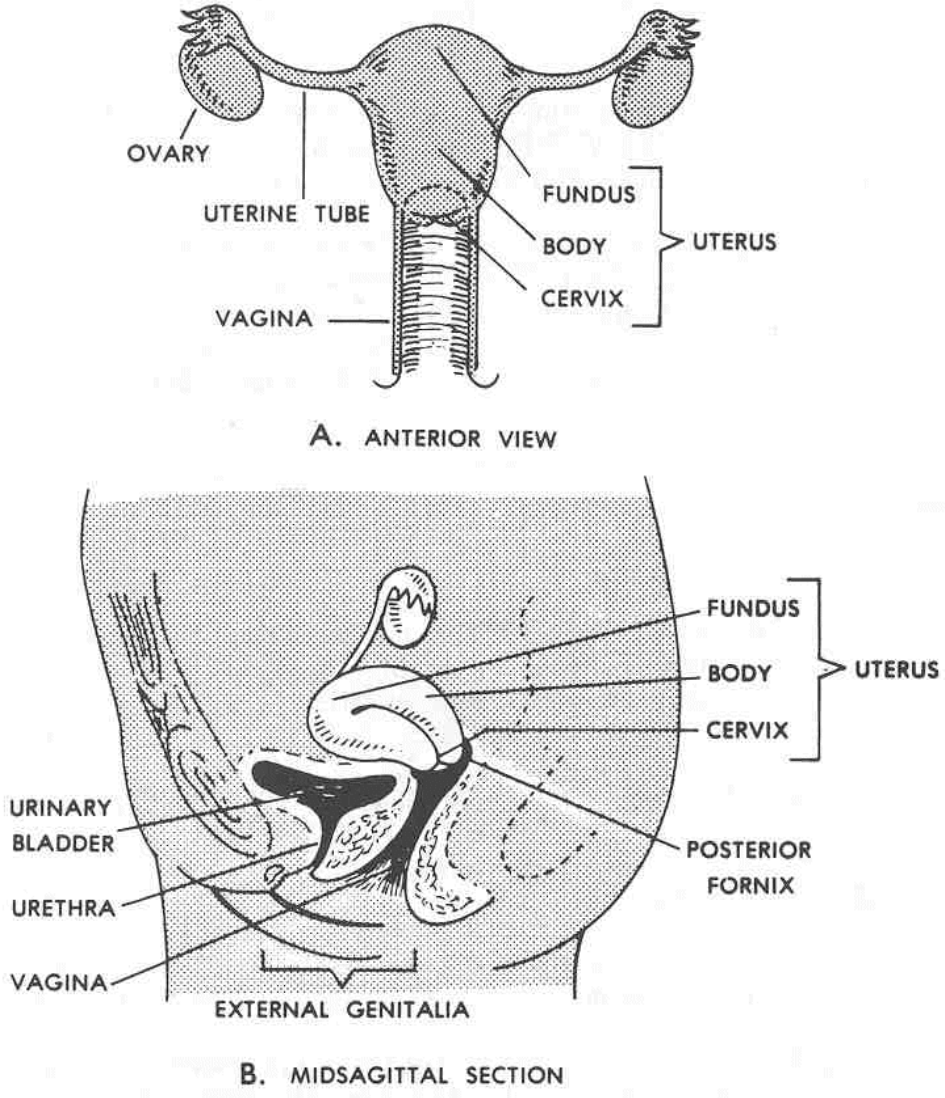


Figure 6-4. The human female genital system.

a. The ovary produces the egg cell or ovum (ova, plural).

b. The ovary produces female sex hormones (estrogens and progesterone).

c. The production of ova is cyclic. Usually, one ovum is released during each 28-day menstrual cycle.

6-15. SECONDARY SEX ORGANS

a. **Uterine Tubes (Fallopian Tubes, Oviducts)**. Extending to either side of the uterus are two muscular tubes, which open at the outer ends like fringed trumpets. The fringe-like appendages encircle the ovaries. At their medial ends, the uterine tubes open into the uterus. The function of the uterine tubes is to pick up the ovum when released from the ovary and hold it UNTIL one of the following happens:

(1) Fertilization. Then it is fertilized. After fertilization, the initial stages of embryo development take place. The developing embryo is eventually moved into the uterus.

(2) Death of Ovum. The nutrient stored within the ovum is used up, and the ovum dies. This may take 3-5 days.

b. **Uterus**. The uterus is the site where all but the first few days of embryo development takes place. After 8 weeks of embryonic development, it is known as the fetus.

(1) Main subdivisions. The uterus is shaped like a pear, with the stem (cervix) facing downward and toward the rear. The fundus is the portion of the uterus above the openings of the uterine tubes. The main part, or body, is the portion between the cervix and the fundus. The uterus usually leans forward with the body slightly curved as it passes over the top of the urinary bladder. The cervix opens into the upper end of the vagina.

(2) Wall structure. The inner lining of the uterus is called the endometrium. Made up of epithelium, it is well supplied with blood vessels and glands. The muscular wall of the uterus is called the myometrium. In the body of the uterus, the muscular tissue is in a double spiral arrangement. In the cervix, it is in a circular arrangement.

(3) Age differences. The uterus of an infant female is undeveloped. During puberty the uterus develops. The uterus of an adult is fully developed. The uterus of an old woman is reduced in size and nonfunctional.

c. **Vagina**. The vagina is a tubular canal connecting the cervix of the uterus with the outside. It serves as a birth canal and as an organ of copulation. It is capable of stretching during childbirth. The low opening of the vagina may be partially closed by a thin membrane known as the hymen.

d. **External Genitalia**. Other terms for the external genitals of the human female are vulva and pudendum. Included are the:

(1) Mons pubis. The mons pubis is a mound of fat tissue covered with skin and hair in front of the symphysis pubis (the joint of the pubic bones).

(2) Labia majora. Extending back from the mons pubis and encircling the vestibule (discussed below) are two folds known as the labia majora. Their construction is similar to the mons pubis, including fatty tissue and skin. The outer surfaces are covered with hair. The inner surfaces are moist and smooth. The corresponding structure in the male is the scrotum.

LABIA = lips (LABIUM, singular)

(3) Labia minora. The labia minora are two folds of skin lying within the labia majora and inclosing the vestibule. In front, each labium minus (minus = singular or minora) divides into two folds. The fold above the clitoris (discussed below) is called the prepuce of the clitoris. The fold below is the frenulum.

(4) Clitoris. The clitoris is a small projection of sensitive erectile tissue that corresponds to the male penis. However, the female urethra does not pass through the clitoris.

(5) Vestibule. The cleft between the labia minora and behind the clitoris is call the vestibule. It includes the urethral opening in front and the vaginal opening slightly to the rear.

e. **Pregnancy and Delivery.** When an embryo forms an attachment to the endometrium, a pregnancy exists. The attachment eventually forms a placenta, an organ joining mother and offspring for such purposes as nutrition of the offspring. The fetal membranes surround the developing individual (fetus), and are filled with the amniotic fluid.

(1) During the first 8 weeks, the developing organism is known as an embryo. During this time, the major systems and parts of the body develop.

(2) During the remainder of the pregnancy, the developing organism is known as the fetus. During this time, growth and refinement of the body parts occur.

(3) Parturition is the actual delivery of the fetus into a free-living state. The delivery of the fetus is followed by a second delivery--that of the placenta and fetal membranes.

f. **Menstruation and Menopause.** About 2 weeks after an ovum is released, if it is not fertilized, menstruation occurs. Menstruation involves the loss of all but the basal layer of the endometrium. This process includes bleeding. It first occurs at puberty and lasts until menopause (45-55 years of age). After menopause, pregnancy is no longer possible.

6-16. SECONDARY SEXUAL CHARACTERISTICS

The secondary sexual characteristics of females include growth of pubic hair, development of mammary glands, development of the pelvic girdle, and deposition of fat in the mons pubis and labia majora.

6-17. MAMMARY GLANDS

Secretion of milk begins after parturition. Stimulation from suckling helps to maintain the normal rate of milk secretion. At the time of menopause, breast tissue becomes less prominent.

Section V. THE HUMAN MALE GENITAL (REPRODUCTIVE) SYSTEM

6-18. PRIMARY SEX ORGANS (TESTES)

The primary sex organ of the human male is the testis. See figure 6-5 for an illustration of the male genital system. The testes are egg-shaped.

a. **Location**. The paired testes lie within the scrotum. The scrotum is a sac of loose skin attached in the pubic area of the lower abdomen. The scrotum provides a site cooler than body temperature to maintain the viability of the spermatozoa (see below). However, when the air is too cold, muscles and muscular fibers draw the testes and scrotum closer to the body to maintain warmth. Otherwise, the scrotum hangs loosely. The tunica vaginalis is a serous cavity surrounding each testis.

b. **Functions.** The testis produces the male sex cells, called spermatozoa (spermatozoon, singular). The millions continuously produce the spermatozoa. One such cell may eventually fertilize an ovum of a human female. The testes also produce male sex hormones, called androgens.

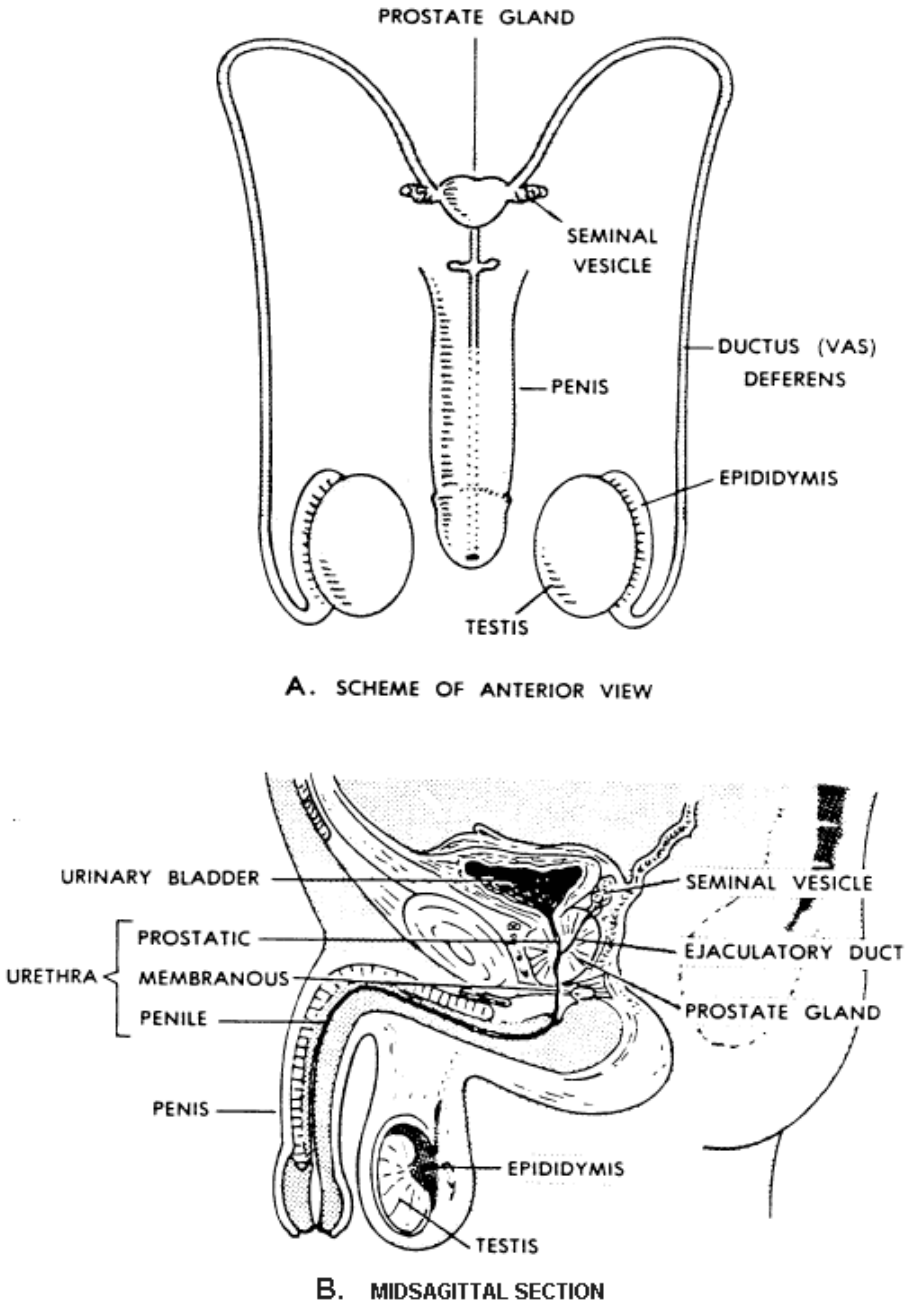


Figure 6-5. The human male genital system.

6-19. SECONDARY SEX ORGANS

a. **Epididymis.** The epididymis is a coiled tube whose function is to aid in the maturation of spermatozoa. Its coiled length is only about 1 1/2 inches. Its uncoiled length is about 16 feet. When coiled, it extends downward along the posterior side of each testis. Its lining secretes a nutritive medium for spermatozoa. It receives spermatozoa from the testes in an immature state. As the spermatozoa pass through the nutrient, they mature**.**

b. **Ductus (Vas) Deferens.** The ductus deferens is a transporting tube that carries the mature sperm from the epididymis to the prostate. Each tube enters the abdomen through the inguinal canal. Each passes over a ureter to reach the back of the urinary bladder and then down to the prostate gland.

c. **Seminal Vesicles**. Lying alongside each ductus deferense as it crosses the back of the bladder is a tubular structure called the seminal vesicle. The seminal vesicle produces a fluid that becomes part of the ejaculate (see below).

d. **Ejaculatory Duct.** Each ductus deferens and its corresponding seminal vesicle converge to form a short tube called the ejaculatory duct. The ejaculatory duct opens into the urethra within the prostate gland (see below). The ejaculatory duct carries both spermatozoa and seminal vesicle fluid**.**

e. **Prostate Gland.** As the urethra leaves the urinary bladder, a chestnut-size gland called the prostate gland surrounds its first inch. The prostate gland provides an additional fluid to be added to the spermatozoa and seminal vesicle fluid.

f. **Penis.** As the urethra leaves the abdomen, it passes through the penis, the male organ of copulation.

(1) Surrounding the urethra is a central cylinder of erectile tissue called the corpus spongiosum. This cylinder is bulb-shaped at each end. The posterior end is attached to the base of the pelvis. The sensitive anterior end is known as the glans.

CORPUS SPONGIOSUM = spongy body

(2) Overlying the corpus spongiosum is a pair of cylinders of erectile tissue called the corpora cavernosa. These two cylinders are separate in their proximal fourth and joined in their distal three-fourths. They are attached to the pubic bones. Together, the corpus spongiosum and the corpora cavernosa combine to form the shaft of the penis.

CORPUS CAVERNOSUM = cavernous body

(3) The prepuce, or foreskin, is a covering of skin for the glans. It may be removed in a surgical procedure called circumcision.

6-20. SECONDARY SEXUAL CHARACTERISTICS

The secondary sexual characteristics of male include growth of facial pubic, and chest hair, growth of the larynx to deepen the voice, and deposition of protein to increase muscularity and general body size.

Continue with Exercises

EXERCISES, LESSON 6

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. Which of the following are components of the human urogenital system? (More than one response may be correct.)

   a. Urinary organs.

   b. Pleural space.

   c. Reproductive organs.

   d. Pituitary gland.

2. Which of the below is a major component of the human urinary system?

   a. Urethra.

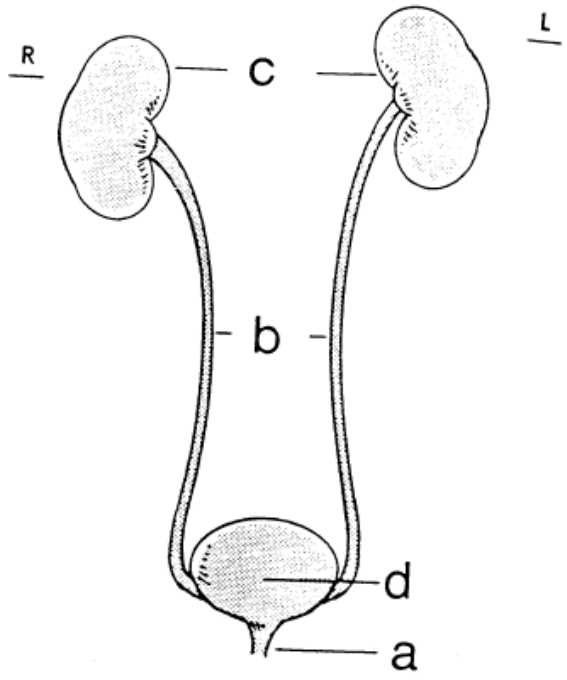
   b. Urinary bladder.

   c. Ureters.

   d. Kidneys.

   e. All the above.

3. Refer to the drawing below. Match the name of each component of the urinary system with its location on the drawing.



____ Ureter

____ Urethra

____ Kidney

____ Urinary bladder

4. Which of the below is a function of the nephron? (More than one response may be correct.)

   a. Remove the wastes of protein usage from the blood.

   b. Remove the secretions of endocrine glands from the blood.

   c. Conserve water and other materials for continued use by the body.

5. Which of the following statements is true concerning the role of the renal tubule?

   a. The renal tubule drains into the renal capsule.

   b. The renal tubule decreases sodium reabsorption when acted on by aldosterone.

   c. The renal tubule selectively removes the wastes of protein usage from the glomerular filtrate.

   d. The renal tubule selectively removes blood cells and large proteins from the glomerular filtrate.

6. The antidiuretic hormone is one of the two main hormones involved in the formation of urine. What is its role in the formation of urine?

    a. The antidiuretic hormone dilutes the concentration of urine by increasing the amount of water reabsorbed in the distal and collecting tubules.

    b. The antidiuretic hormone dilutes the concentration of the urine by increasing sodium reabsorption in the distal tubules and collecting ducts.

    c. The antidiuretic hormone concentrates the urine by decreasing sodium and water absorption in the distal tubules and collecting ducts.

    d. The antidiuretic hormone increases water absorption in order to concentrate the urine.

7. The ureter can be described as a tube that:

    a. Conducts the urine from the urinary bladder to the outside of the body.

    b. Allows for reabsorption of water from the glomerular filtrate in order to concentrate the urine.

    c. Connects the kidneys to the urinary bladder.

    d. Collects the urine after it has passed through the distal convoluted tubule.

8. Uremia is a condition-characterized by:

    a. An inflammation of the nephrons caused by toxic material produced by certain bacteria.

    b. A build-up of toxic substances in the blood because of kidney failure.

    c. Increased urine output due to a low production of the antidiuretic hormone.

    d. A burning and stinging sensation in the urinary bladder due to some type of chronic inflammation.

9. What is the primary sex organ in the human female?

    a. The ovary.

    b. The vagina.

    c. The uterus.

    d. The cervix.

10. The vagina is best described as:

    a. A mound of fat tissue covered with skin and hair in front of the symphysis pubis.

    b. A small projection of sensitive erectile tissue which corresponds to the male penis.

    c. A tubular canal that connects the cervix of the uterus with the outside.

    d. The cleft between the labia minora and behind the clitoris.

11. The primary sex organ in the human male is the:

    a. Epididymis.

    b. Penis.

    c. Seminal vesicle.

    d. Testis.

12. What is the function of the testis?

    a. Production of androgens.

    b. Production of estrogens.

    c. Production of spermatozoa.

    d. Production of a fluid that retards the development of spermatozoa.

    e. All the above.

    f. b and d only.

    g. a and c only.

13. The prostate gland:

    a. Provides an additional fluid that is added to the spermatozoa and seminal vesicle fluid.

    b. Is the gland that produces spermatozoa.

    c. Is a coiled gland that secretes a nutritive medium for spermatozoa so they mature.

    d. Is the tissue responsible for the production of the male sex hormones called androgens.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 6

1. a (para 6-1)
   c (para 6-1)

2. e (para 6-4b)

3. b Ureter
   a Urethra
   c Kidney
   d Urinary bladder
   (figure 6-1)

4. a (para 6-5c)
   c (para 6-5c)

5. c (para 6-5c)

6. d (para 6-6a)

7. c (para 6-7a)

8. b (para 6-10a)

9. a (para 6-14)

10. c (para 6-15d)

11. d (para 6-18)

12. g (para 6-18b)

13. a (para 6-19e)

End of Lesson 6

LESSON ASSIGNMENT

SUBCOURSE MD0806 Therapeutics III.

LESSON 7 Antihypertensive Agents.

LESSON ASSIGNMENT Paragraphs 7-1--7-12.

LESSON OBJECTIVES After completing this lesson you will be able to:

7-1. From a group of statements, select the statement which best defines the term essential hypertension.

7-2. Given the name of a type of essential hypertension and a group of statements, select the statement that best describes that type.

7-3. Given a group of statements, select the statement that best describes why diuretics are used to treat hypertension.

7-4. Given a group of trade and/or generic names of antihypertensive agents match each trade name with its corresponding generic name.

7-5. Given the trade and/or generic name of an antihypertensive agent and a group of indications, side effects, or patient warnings; select the indication(s), side effect(s), or patient warning(s) associated with that agent.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 7

ANTIHYPERTENSIVE AGENTS

Section I. INTRODUCTION TO HYPERTENSION

7-1. INTRODUCTION

a. It is estimated that 23 million people in the United States suffer from hypertension. Of this number, it is thought that 11.5 million people have been diagnosed as having the condition and that 5.75 million of those people are being treated for it. Unfortunately, it is estimated that only 2.875 million of those persons treated for hypertension are being treated properly. Therefore, it is obvious that hypertension is a major medical problem which should be a concern of all medical personnel.

b. Hypertension (high blood pressure) is prevalent in both men and women. It frequently contributes to the death of many persons. The cause of most cases of hypertension is unknown. This type of hypertension is referred to as primary or essential hypertension. Hypertension that has a known cause (kidney disease, hyperthroidism) is called secondary hypertension. Blood pressure is the force that the blood exerts on the vessel wall while the heart is contracting and at rest. The force against the vessel wall during contraction or systole is the systolic pressure and the force during rest or diastole is the diastolic pressure. The blood pressure is expressed in terms of millimeters of mercury (Hg). Normal blood pressure is less than 135 mm Hg (systolic) and less than 85 mm Hg (diastolic) = 135/85 mm Hg.

7-2. TREATMENT OF HYPERTENSION

There is no cure for hypertension. Most patients who have a bacterial infection are accustomed to taking a 10-day treatment regimen of an antibiotic in order to rid themselves of the infection. The same is not true with hypertension. Once a person begins taking an antihypertensive agent, it is likely that he will continue taking some type of antihypertensive agent for the rest of his life.

7-3. DEFINITION OF ESSENTIAL (PRIMARY) HYPERTENSION

Essential (primary) hypertension can be defined as a disorder of unknown origin characterized mainly by an elevated systolic or diastolic blood pressure associated with generalized arteriolar vasoconstriction (see Lesson 3). Essential hypertension may be divided into three classes according to the severity of the condition. Labile hypertension is a condition of elevated blood pressure with intervening periods of normal blood pressure.

7-4. CLASSES OF ESSENTIAL HYPERTENSION

a. **Stage I Hypertension**. Stage I hypertension is characterized by sustained, documented systolic pressure 140 to 159 mm Hg and/or diastolic pressure measurements 90 to 99 mm Hg. Signs of this type include increased heart rate (tachycardia) and increased cardiac output with normal total peripheral vascular resistance; however, the majority of patients cannot tell that they have hypertension.

b. **Stage II Hypertension**. Stage II hypertension is characterized by sustained, systolic elevation (160 to 179 mm Hg) and/or diastolic pressure (100 to 109 mm Hg). Symptoms are the same as noted in Stage I. Patients with Stage I or II DO NOT show signs of target end organ damage. The organs of most concern are the heart, kidneys, and eyes. Stage I and II hypertension may be treated nonpharmacologically with diet and exercise or pharmacologically with anti-hypertensive medications.

c. **Stage III Hypertension**. Stage III hypertension is characterized by a persistent elevation (systolic greater than 180 mm Hg; diastolic greater than 110 mm Hg) with target end organ damage. Damage to the heart may include strain or enlargement of the left ventricle. Kidney damage may appear as abnormal laboratory values that indicate inefficiency. Damage to the eyes may appear as small hemorrhages due to the sustained blood pressure in these small vessels. This stage is often treated immediately with anti-hypertensive medications.

d. **Hypertensive Urgency/Crisis.**

(1) Hypertensive urgency is a condition of persistent elevation in blood pressure without target end organ damage. However, the pressure is high enough that the patient presents for treatment because of symptoms of dizziness, chest pain, or confusion. The goal in treatment of this condition is to normalize the blood pressure as quickly as possible (usually over 1 to 3 days).

(2) Hypertensive crisis is a similar condition. However, the patient has symptoms of target end organ damage. This may be a life-threatening condition. The goal of therapy is to normalize the blood pressure in 12 to 24 hours. Both conditions are usually treated with intravenous (IV) anti-hypertensives.

7-5. REVIEW OF IMPORTANT FACTORS RELATING TO HYPERTENSION

Essential hypertension is a process of variable course and severity. Several options are open to the physician depending upon the severity of the drug therapy. Condition weight reduction and diet control may be adequate treatment; however, drug therapy is sometimes needed. When drug therapy is required, it usually begins with a diuretic followed by the addition of the other agents based on the patient's response. However, certain classes of drugs may be more advantages (less side effects) when patients have other diseases. It is not unreasonable to see patients treated by the same provider on different drugs.

7-6. DIURETICS IN THE TREATMENT OF HYPERTENSION

The effectiveness of diuretics in the treatment of essential hypertension arises from the fact that diuretic agents decrease tubular reabsorption of sodium, which caused a reduction in blood pressure. Some of the common diuretics include hydrochlorothiazide, spironolactone (Aldactone®), furosemide (Lasix®), and triamterene (Dyrenium®). These agents will be discussed in detail in Lesson 8 of this subcourse.

7-7. COMBINATION THERAPY IN THE TREATMENT OF HYPERTENSION

When diuretics alone are ineffective in controlling hypertension, it is necessary to combine the diuretic therapy with one or more additional agents. The physician may use many combinations of agents in order to control the patient's high blood pressure. The patient should be encouraged to discuss any questions he might have concerning the side effects (for example, drowsiness), which might be caused by an agent or agents.

Section II. DRUGS USED IN THE TREATMENT OF HYPERTENSION

NOTE: For this discussion commonly used antihypertensive agents will be classified into the following categories.

7-8. DRUGS WHICH ACT ON THE SYMPATHETIC NERVOUS SYSTEM

NOTE: For a review of the sympathetic nervous system, refer to Subcourse MD0805, Therapeutics II.

a. **Methyldopa (Aldomet®).** Methyldopa is one of the drugs of this type. It is believed to produce its effects by its being metabolized to a substance which is very similar to norepinephrine--but with considerably less vasoconstricting activity than is shown by epinephrine. Thus, methyldopa competes with norepinephrine and thereby depresses the activity of the sympathetic nervous system. This medication is rarely used, but is still one of the drugs of choice for pregnancy-induced hypertension. Side effects associated with this agent include bradycardia, swelling of the feet and lower legs (because sodium and water retention), drowsiness, and mental depression.

b. **Clonidine (Catapres®, Catapres TTS®).** Clonidine is an agent that is believed to act by decreasing sympathetic outflow from the brain and consequently inhibit vasoconstriction. It is used in mild to moderate hypertension. Side effects associated with this agent include swelling of the feet and lower legs (due to sodium and water retention) and mental depression. The patient taking this drug should be cautioned to check with his physician before suddenly discontinuing the medication because abrupt withdrawal from the drug may cause serious hypertension problems. Clonidine is also used in the treatment of symptoms associated with alcohol withdrawal.

7-9. BETA ADRENERGIC BLOCKERS

Beta adrenergic blocking agents block the effect of the sympathetic neurotransmitters by competing for receptors.

a. **Propranolol (Inderal®)**. Propranolol is a drug used in the treatment of hypertension, angina pectoris, and cardiac arrhythmias. Side effects associated with propranolol include dizziness, mental confusion, and mental depression. It may also exacerbate congestive heart failure and mask the symptoms of hypoglycemia.

b. **Metaprolol (Lopressor®, Toprol XL®).** Metaprolol is prescribed for the same conditions as propranolol and is also indicated used in the treatment of myocardial infarction and treatment of congestive heart failure. Normal doses for hypertension are 25 – 100mg twice daily. The dose for heart failure is 6.25 to12.5 mg twice daily and adjusted upward as tolerated by the patient. This agent is available as an oral and injectable preparation.

c. **Other Beta Adrenergic Blockers**. Other beta blockers used in the treatment of hypertension include betaxolol (Kerlone®), bisoprolol (Zebeta®), labetolol (Trandate®, Normodyne®), nadolol (Corgard®), and carvedilol (Coreg®). Carvedilol is also indicated for congestive heart failure.

7-10. SMOOTH MUSCLE RELAXANTS

Drugs in this category treat hypertension by acting directly on vascular smooth muscle by relaxing the blood vessels. Consequently, they cause vasodilation and a decrease in peripheral resistance results in a lower blood pressure.

a. **Hydralazine (Apresoline®).** Hydralazine is given orally or injected in the management of hypertension. Preferably, it is used in conjunction with other antihypertensive agents. Side effects associated with this agent include chest pain (angina pectoris), a general feeling of weakness, unexplained sore throat, joint pain, and headache. The patient should to be told to avoid getting up suddenly from a lying or a sitting position.

b. **Alpha Adrenergic Blockers**. Alpha adrenergic blockers block alpha receptors in peripheral vessels, therefore causing vasodilation. Agents in the class include prazosin (Minipress®), doxazosin (Cardura®), and terazosin (Hytrin®). Doxazosin and terazosin offer the advantage of once daily dosing and the added benefit of relieving the symptoms of benign prostatic hyperplasia (enlarged prostate gland). Dizziness, drowsiness, and headache are common side effects associated with these agents, especially with the first dose. Patients must be counseled on these side effects and instructed to take the first dose in the evening at home. Some patients who have taken this drug have also experienced syncope (unconsciousness due to decreased oxygen supply to the brain).

c. **Calcium Channel Blockers**. Calcium channel blockers are potent peripheral vasodilators used in the treatment of hypertension. They are similar to beta blockers that can slow the heart rate. Calcium channel blockers are also used in the treatment of atrial fibrillation to control the heart rate. Many of the products are available in oral and injectable form and may be administered once daily. Side effects include dizziness, headache, heartburn, edema, and constipation. Agents include diltiazem (Cardizem®, Tiazac®, Dilacor®), verapamil (Calan®, Isoptin®, Covera®, Verelan®), amlodipine (Norvasc®), felodipine (Plendil®), and nifedipine (Procardia XL®, Adalat CC®).

d. **Angiotensin Converting Enzyme Inhibitors (ACE Inhibitors).** ACE inhibitors work by inhibiting the enzyme which converts angiotensin I to angiotensin II. Angiotensin II is one of the most potent vasoconstrictors known to man. By inhibiting the enzyme, these agents produce vasodilation and are used in the treatment of hypertension and congestive heart failure. Most products are administered one to two times daily. The most common side effects are rash, dry cough, and hyperkalemia. These agents are contraindicated in pregnancy. Selected agents include benazepril (Lotensin®), captopril (Capoten®), enalapril (Vasotec®), lisinopril (Prinivil®, Zestril®), and ramipril (Altace®). Enalapril is available in an injectable form.

e. **Angiotensin II Receptor Blockers (ARBs).** ARBs work by directly blocking the angiotensin II receptor to cause vasodilation and lower blood pressure. They appear to have less side effects than ACE inhibitors, especially the dry cough. Selected agents include irbesartan (Avapro®), losartan (Cozaar®), and valsartan (Diovan®).

7-11. COMBINATION PRODUCTS

It should be apparent that in order to control hypertension the patient may be required to take extremely large amounts of medication. In an attempt to develop a more convenient method of controlling hypertension, researchers have combined diuretic and antihypertensive agents in order to maximize the best attributes of each. These combination products are very convenient for the patient to use if the dosage of the product is exactly what the patient needs to control his hypertension. Since these combination products tend to be rather expensive, military pharmacies frequently have a limited selection of these items in stock. Two examples of combination products are listed below.

a. **Aldactazide® (Spironolactone and Hydrochlorothiazide).** Spironolactone and hydrochlorothiazide are both diuretics. This particular drug is used in the treatment of hypertension, congestive heart failure and cirrhosis of the liver. The patient taking this medication should be told to take the preparation with or after meals to minimize stomach upset.

b. **Dyazide® (Triamterene and Hydrochlorothiazide).** Triamterene and hydrochlorothiazide are both diuretics. This product is used as a diuretic and as an antihypertensive agent.

7-12. THE TREATMENT OF A HYPERTENSIVE CRISIS OR EMERGENCY

Patients presenting with extreme elevations of blood pressure and symptoms of impending stroke, pulmonary edema, kidney failure, or heart attack must be promptly. The following agents are used to treat hypertensive crisis:

a. **Diazoxide (Hyperstat® I.V.)** This agent is administered by rapid intravenous (I.V.) injection (150 to 300 milligrams immediately, repeated in 30 minutes and every four hours if needed). When administered, this agent produces a fall in blood pressure in from one to five minutes. Hyperglycemia and sodium retention are side effects associated with this agent.

b. **Nitroprusside (Nipride®).** Nitroprusside is administered by continuous intravenous infusion at a rate of 0.5 to 0.8. micrograms per kilogram of patient weight per minute. The patient must be closely observed when he is receiving this drug since overdosage of nitroprusside results in cyanide poisoning. Nitroprusside is not intended for direct injection. Instead, the drug must be used as an infusion with sterile 5 percent dextrose in water. The intravenous infusion must be used within four hours once it is prepared. Furthermore, the prepared intravenous infusion must be protected from light (for example, the bottle wrapped with foil). Nausea, vomiting, and headache are side effects commonly associated with this agent.

Continue with Exercises

EXERCISES, LESSON 7

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. Match the drug name in Column A with its trade name listed in Column B.

COLUMN A	COLUMN B
_____ Lisinopril.	a. Cardura®.
_____ Spironolactone and hydrochlorothiazide combination.	b. Catapres®.
_____ Doxazosin.	c. Adalat CC®.
_____ Diltiazem.	d. Inderal®
_____ Metoprolol.	e. Calan®.
_____ Propranolol.	f. Cardizem®.
_____ Clonidine.	g. Zestril®.
_____ Verapamil.	h. Lopressor®.
_____ Nifedipine.	i. Aldactazide®.

2. Which of the following statements best defines the term essential hypertension?

   a. A disorder of unknown origin characterized mainly by an elevated systolic or diastolic pressure associated with generalized arteriolar vasoconstriction.

   b. A disorder caused by too many fats in the diet and by an excess of sodium in the intracellular fluid.

   c. A disorder produced by unknown causes which results in a diastolic pressure which is higher than the systolic pressure.

   d. A disorder of unknown origin that can be cured by a 10-day treatment regimen of diuretics and antihypertensives.

3. Which of the following statements best describes Stage I primary hypertension?

   a. A type of essential hypertension characterized by documented pressure measurements greater than159 mm Hg (systolic) and / or greater than 99 mm Hg (diastolic).

   b. A type of essential hypertension characterized by a persistent elevation in diastolic pressure with minor target organ (heart and kidney damage).

   c. A type of essential hypertension characterized by marked elevated blood pressure with definite target organ (heart and kidney) damage.

   d. A type of essential hypertension characterized by a mild, but sustained, elevation in diastolic pressure without target organ (heart and kidney) damage.

4. Stage III primary hypertension is best described as a type of essential hypertension characterized by:

   a. Persistent elevated diastolic pressure with minor damage to the heart and/or kidneys.

   b. Documented diastolic pressure associated with generalized arteriolar vasoconstriction.

   c. A mild, but sustained, elevation in diastolic pressure without damage to the heart and/or kidneys.

   d. Marked elevated blood pressure with definite damage to the heart and/or kidneys.

5. Nitroprusside (Nipride®) is used in the treatment of:

    a. Essential hypertension.

    b. Hypertensive crisis.

    c. Labile primary hypertension.

    d. Moderate primary hypertension.

6. What side effect is associated with beta blockers?

    a. Swelling of the feet and lower legs.

    b. Tachycardia.

    c. Restlessness.

    d. Mask symptoms of hypoglycemia.

7. What should the patient taking terazosin be told?

    a. To be aware that many patients taking the drug experience impotence or decreased sexual interest.

    b. To take the medication one hour before meals in order to increase the absorption of the drug.

    c. To arise slowly from a lying or sitting position because of the possibility of orthostatic hypotension and syncope.

    d. To avoid taking the medication with fats because absorption of the drug is affected.

8. The patient taking nitroprusside should be closely monitored because:

   a. Hyperglycemia and sodium retention occur so abruptly with this agent that death can result if the drug is not withdrawn after their onset.

   b. Overdosage of nitroprusside results in cyanide poisoning.

   c. Abrupt withdrawal of this agent can result in an extreme hypertensive crisis.

   d. Too rapid administration of this product can result in a cerebrovascular accident.

9. Which of the following is a side effect associated with the use of enalapril?

   a. Hypokalemia (low potassium).

   b. Dry cough.

   c. Syncope.

   d. Chest pain.

10. What is an indication for Coreg®?

   a. Antihypertensive.

   b. Congestive heart failure.

   c. Antianginal agent (treatment of angina pectoris).

   d. a and b only.

   e. a, b, and c.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 7

1.	___G.__ Lisinopril (para 7-10d).	a. Cardura®.
	___I.___ Spironolactone and hydrochlorothiazide combination. (para 7-11a)	b. Catapres®
	___A__ Doxazosin (para 7-10b).	c. Adalat CC®
	___F__ Diltiazem (para 7-10c).	d. Inderal®
	___H__ Metoprolol (para 7-9b).	e. Calan®
	___D__ Propranolol (para 7-9a).	f. Cardizem®
	___B__ Clonidine (para 7-8b).	g. Zestril®
	___E__ Verapamil (para 7-10c).	h. Lopressor®
	___C__ Nifedipine (para 7-10c).	i. Aldactazide®

2. a (para 7-3)
3. a (para 7-4a)
4. d (para 7-4c)
5. b (para 7-12b)
6. d (para 7-9a)
7. c (para 7-10b)
8. b (para 7-12b)
9. b (para 7-10d)
10. d (para 7-9c)

End of Lesson 7

LESSON ASSIGNMENT

SUBCOURSE MD0806 Therapeutics III.

LESSON 8 Diuretic and Antidiuretic Agents.

LESSON ASSIGNMENT Paragraphs 8-1--8-7.

LESSON OBJECTIVES After you finish this lesson you should be able to:

8-1. Given a group of statements, select the statement that best defines the term diuretic.

8-2. Given a list of conditions, select the condition(s) that are treated with diuretic therapy.

8-3. Given the name of a type of diuretic and a group of statements describing the mechanisms of action of different types of diuretics, select the mechanism of action for that type of diuretic.

8-4. Given the trade and/or generic name of a diuretic agent or antidiuretic agent and a list of indications, uses, side effects, or precautionary statements, select the indication(s), use(s), side effect(s), or precautionary statements(s) for that particular agent.

8-5. Given a group of trade and/or generic names of various diuretic or antidiuretic agents match each trade or generic name with its corresponding trade or generic name.

8-6. Given the trade or generic name of a diuretic agent and a list of types of diuretic agents select the type of diuretic to which that agent belongs.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 8

DIURETIC AND ANTIDIURETIC AGENTS

Section I. DIURETIC AGENTS

8-1. INTRODUCTION

In Lesson 3 of this subcourse, congestive heart failure was described as a condition characterized by sodium retention that results in expanded extracellular fluid volume or edema. This same process of increased tubular reabsorption of sodium-resulting in an accumulation of fluid--may accompany cirrhosis of the liver, renal disease, toxemia of pregnancy, the side effects of drugs, and other states of fluid retention. In all of these conditions, treatment of sodium retention is what is desired. REMEMBER: WHERE SODIUM GOES, WATER GOES! Therefore, the treatment as sodium retention by sodium excretion--not just the increase in urine volume--is the desired goal. Diuretic agents increase the amount of sodium excreted from the body.

8-2. DEFINTION OF DIURETIC

A diuretic is any agent that produces diuresis (an increase in the volume of urine output that results in the mobilization of edema fluid). You have heard the term edema before. Edema is the presence of abnormally large amounts of fluid in the body. Many diuretics reduce edema by increasing the amount of sodium removed from the body. Remember, where sodium goes, water goes. Thus, when sodium is removed from the body, there is a corresponding increase in the volume of urine produced.

8-3. USES OF DIURETICS

The general uses of diuretics include the treatment of congestive heart failure, hypertension, glaucoma, ascites, toxemia of pregnancy, and diabetes insipidus. Congestive heart failure has been discussed in Lesson 3 of this subcourse, hypertension has been discussed in Lesson 7 of this subcourse, and glaucoma has been discussed in MD0805, Therapeutics II. Review these materials if you have a need. The other conditions will be explained in this paragraph. Ascites is the accumulation of fluid in the abdominal cavity. Toxemia of pregnancy is a group of pathologic conditions--essentially metabolic disturbances--which sometimes occurs in pregnant women. Toxemia of pregnancy is manifested by preeclampsia (a toxemia of late pregnancy characterized by hypertension, albuminuria, and edema) and fully developed eclampsia (this condition includes convulsions and coma, which might occur in a pregnant woman or in a woman who has just delivered). Hypertension, edema, and/or proteinuria characterize eclampsia. Diabetes insipidus is a metabolic disorder caused by a lack of production of antidiuretic hormone (ADH), which is marked by great thirst and the passage of a large amount of dilute urine with no excess of sugar.

8-4. TYPES OF DIURETICS

There are several types of diuretics. The categories are defined based upon their mechanism of action.

a. **Osmotic Diuretics**.

(1) General. Osmostic diuretics produce a diuresis of water rather than a diuresis of sodium. The body does not metabolize osmotic diuretics. Instead, the drug molecules are not reabsorbed in the kidney tubules. This greatly affects the tonicity of every part of the kidney tubules through which the glomerular filtrates pass. By the process of osmosis, the drug molecules draw an increased amount of water from the interstitial fluid compartment. The result is that a great volume of urine is produced (water diuresis). Sodium is contained in that urine and is subsequently removed from the body. Thus, the osmotic diuretics indirectly produce a removal of sodium from the body.

(2) Mannitol. Mannitol is used to prevent acute renal (kidney) failure, evaluate kidney functioning, treat glaucoma (by the reduction of intraocular pressure), promote the urinary excretion of toxic substances (diuresis in certain drug intoxications) and reduce intracranial pressure (pressure in the head). The usual dosage of mannitol is from 50 to 200 grams in a 24-hour period by intravenous infusion. Side effects associated with the use of mannitol include pulmonary congestion, fluid and electrolyte imbalance, acidosis, electrolyte loss, and dryness of mouth and dehydration. Since mannitol may crystallize on exposure to low temperatures, you should observe mannitol vials and premixed bags for such crystals. When you observe these crystals, you should warm the vials or bags in a 50ºC water bath in order to dissolve the crystals. The product should be cooled to body temperature before the mannitol solution is administered. Mannitol is available in a 5, 10, 15, 20, and 25 percent injection.

b. **Thiazide Diuretics.** Thiazide diuretics work by the inhibition of sodium reabsorption in the first portion of the distal tubule. The passive diffusion of the accompanying water and chloride is correspondingly reduced. Thus, the result is an increased excretion of sodium, water, and chloride from the body. When the thiazide acts on the proximal tubule, the carbonic anhydrase activity in the distal tubule is also decreased. This causes increased secretion of potassium. Consequently, the water lost contains sodium, potassium, and chloride. This loss of potassium can present problems to the patient.

(1) Hydrochlorothiazide (Hydrodiuril®). Hydrochlorothiazide is used in the treatment of essential hypertension and edema found in congestive heart failure. The usual dose of this drug is from 12.5 to 100 milligrams per day. Side effects commonly associated with hydrochlorothiazide include hypokalemia, hyperglycemia, and hyperuricemia. This drug should be used in caution in patients suffering from diabetes or gout and in patients who take digitalis.

(2) Chlorothiazide (Diuril®). This drug is used as a diuretic and as an antihypertensive. It is available in both parenteral and oral dosage forms. For side effects, refer to hydrochlorothiazide.

(3) Chlorthalidone (Hygroton®). Although chlorthalidone is not the same chemically as the thiazide diuretics, it has the same effects as these agents. For indications and side effects, you should refer to hydrochlorothiazide.

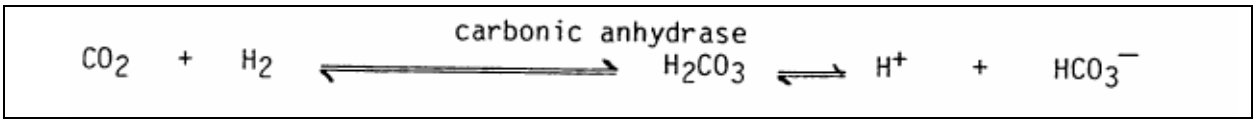
c. **Potassium-Sparing Diuretics**. This type of diuretic is used when there is a need to maintain normal levels of potassium in the patient along with the diuresis. The specific mechanisms of actions of selected drugs in this category are given below.

(1) Spironolactone (Aldactone®). Spironolactone causes sodium diuresis and potassium retention by acting as an aldosterone competitive antagonist. That is, this drug acts on the distal tubule to block the sodium-potassium exchange mechanism. The net result is sodium loss and potassium retention. Consequently, by antagonizing aldosterone, sodium as well as water diuresis and potassium retention are affected. Spironolactone is used for primary hyperaldosteronism, edema associated with congestive heart failure, cirrhosis of the liver or ascites, essential hypertension, and in hypokalemia when other means are considered inappropriate or inadequate. The usual dose of this drug is from 25 to 400 milligrams per day depending upon the condition of the patient. Although spironolactone is a mild diuretic, it can hasten major side effects such as gastrointestinal symptoms (for example: cramping and diarrhea), lethargy, hyperkalemia, and hyponatremia. Hyperkalemia is a major side effect that occurs in patients who have impaired renal function. Hyperkalemia can cause irregularities that may be fatal. Spirolactone also causes estrogen-like side effects because of its hormone-like structure.

(2) Triamterene (Dyrenium). While triamterene produces effects similar to those of spironolactone, the effects produced by triamterene are not dependent on the presence of aldosterone. This agent acts directly on the distal tubule where it prevents the passage of sodium across the membrane of the tubule. Thus, by blocking sodium reabsorption, potassium loss is reduced. Triamterene is used for edema associated with congestive heart failure and cirrhosis of the liver. The usual dosage of this drug is from 25 to 200 milligrams per day. The daily dose should not exceed 300 milligrams. Side effects associated with this agent include electrolyte imbalances, hyperkalemia, weakness, and dry mouth. Like spironolactone, hyperkalemia is a major side effect which can occur in patients who have impaired renal function or when the drug is administered alone.

d. **Carbonic Anhydrase Inhibitor Diuretics**.

(1) Carbonic anhydrase inhibitors produce diuresis by inhibiting carbonic anhydrase in the renal tubules. Carbonic anhydrase is an enzyme that catalyzes the following reaction.



(2) From the reaction above, it can be deduced that removal of or blocking the enzyme carbonic anhydrase would result in a much slower reaction. Consequently, there would be a greatly reduced production of hydrogen ions and bicarbonate ions. This interferes with the ion exchange mechanism at the distal tubule, where the sodium ion that accompanies the bicarbonate ion is reabsorbed only by exchange for hydrogen or potassium ions secreted into the tubule. Normally the bicarbonate ion that accompanies the sodium ion (provided by the glomerular filtrate) is reabsorbed almost complete at the distal tubule. With reduced production of hydrogen ion due to inhibition of the carbonic anhydrase, the bicarbonate ion, together with the sodium ion will not be reabsorbed. Thus, the sodium will be excreted in an unusually large amount--with a corresponding loss of water (remember, where sodium goes, water goes).

(3) Acetazolamide (Diamox®) is one example of a carbonic anhydrase inhibitor. Although rarely used today, it may be used in the treatment of edema because of congestive heart failure; drug-induced edema; petit mal and unlocalized seizures; and open-angle and secondary glaucoma. The usual dosage of this drug ranges from 250 milligrams to 2 grams--depending on the type of condition being treated. Actually, the dosage recommendations for glaucoma and epilepsy differ considerably from those of congestive heart failure, since the first two conditions are not dependent on carbonic anhydrase inhibition in the kidney which requires intermittent dosage if it is to recover from the inhibitory effect of the therapeutic agent. The side effects of this agent include loss of appetite, transient myopia (nearsightedness), drowsiness, and acidosis. Acetazolamide is available in the injectable form.

e. **Inhibition of Sodium Transport in the Ascending Limb of the Loop of Henle, the Distal Tubule, and the Proximal Sites Diuretics**. Diuretics of this type are extremely potent and rapidly acting. In fact, they are used only after less potent--but safer--diuretics have failed. As the category type states, this type of diuretic acts by inhibiting sodium transport in the ascending limb of the loop of Henle, the distal tubule, and in the proximal sites. Thus, a greater fraction of filtered sodium can escape reabsorption. Thereby, increased sodium and water excretions occur. Diuretics of this type are called “loop diuretics”.

(1) Furosemide (Lasix®). Furosemide is used in the treatment of edema associated with congestive heart failure, cirrhosis of the liver and renal disease, pulmonary edema, and hypertension. It is particularly useful when an agent with a greater diuretic potential than that of those commonly used is desired. This agent is also a rapidly acting diuretic. When administered orally it acts within one hour. When administered by injection it acts within 5 to 10 minutes. However, the agent does produce massive changes in electrolyte and water balance in the body. The usual dosage of furosemide is 20 to 80 milligrams given in a single dose--preferably in the morning. Depending on the patient's response, this dose can be repeated, maintained, or reduced. There are numerous adverse effects associated with the use of furosemide. These adverse effects include hypokalemia, hyponatremia, hyperglycemia, electrolyte depletion, and hypovolemia. Reversible and irreversible hearing impairment and loss may occur with any of the loop diuretics. It is often associated with rapid infusion and the use of extremely high doses. The injectable form of the drug must be stored at controlled room temperature and should not be used if the solution is yellow. The oral solution and tablet preparations should be dispensed in light--resistant containers.

(2) Other loop diuretics. Other loop diuretics include bumetanide (Bumex®), ethacrynic acid (Edecrin®), and torsemide (Demadex®).

f. **Inhibition of Sodium and Chloride Reabsorption Diuretics**.

(1) General. The mechanism of action of this type is very similar to the thiazide diuretics. That is, drugs of this category inhibit sodium and chloride reabsorption that results in the increased excretion of sodium, chloride, and water.

(2) Chlorthalidone (Hygroton®). This agent differs from the thiazide diuretics only in chemical structure. Chlorthalidone's pharmacological action is indistinguishable from the thiazide diuretics. Chlorthalidone is used in the management of hypertension--either as the sole therapeutic agent or to enhance the effect of other antihypertensive drugs in patients who have the more severe forms of hypertension. It is also used as adjunctive therapy in the treatment of edema associated with congestive heart failure, hepatic cirrhosis, and various forms of renal dysfunctions. Refer to the information on hydrochlorothiazide for side effect information.

g. **Combination Diuretics (Potassium--Sparing and Thiazide Diuretic Combination).** The potassium--sparing and thiazide diuretics have different but complementary mechanisms and sites of action. Therefore, when given together they produce additive diuretic and antihypertensive effects. The thiazide component blocks the reabsorption of sodium and chloride ions and thus increases the quantity of sodium traversing the distal tubule and the volume of water excreted in the urine. This characteristically induces potassium loss. The potassium-sparing component inhibits the reabsorption of sodium in exchange for potassium and hydrogen ions at the distal tubule so that sodium excretion is greatly favored and the excess loss of potassium, as well as hydrogen and chloride ions induced by the thiazide, is reduced.

(1) Aldactazide® (combination of spironolactone and hydrochlorothiazide). This drug is used for the treatment of edema associated with congestive heart failure, cirrhosis of the liver and ascites and for essential hypertension.

(2) Dyazide® (combination of triamterene and hydrochlorothiazide). This agent is used in the treatment of edema associated with congestive heart failure, cirrhosis of the liver, and hypertension. The usual dosage of this product is from 1 to 2 capsules taken twice daily after meals. The patient should take no more than four capsules per day. The side effects associated with this agent include hyperglycemia, hyperuricemia, and gastrointestinal disturbances. Each Dyazide® capsule contains 37.5 milligrams of triamterene and 25 milligrams of hydrochlorothiazide. There are other combinations of these diuretics available as generics or as Maxide® (75/50; 50/25). One must be very careful and double check the active ingredients to ensure that the correct product is dispensed.

Section II. ANTIDIURETIC AGENTS

8-5. INTRODUCTION

The antidiuretic hormone has been discussed in Lesson 8 of this subcourse. As you will remember, it is a hormone secreted by the pituitary gland. The antidiuretic hormone (ADH) acts on the distal tubule and collecting ducts to increase water reabsorption (and thus to decrease urine output). The agents discussed below are those that work in a manner opposite the diuretics. This process is called antidiuresis. Antidiuresis is the suppression of urinary secretion. Consequently, an antidiuretic is an agent that suppresses urine formation as well as the rate of urine formation.

8-6. MECHANISM OF ACTION OF ANTIDIURETICS

Antidiuretics work by increasing the reabsorption of water at the distal tubule and collecting ducts without significantly modifying the rate of glomerular filtration.

8-7. EXAMPLES OF ANTIDIURETIC AGENTS

Two examples of antidiuretic agents are presented below.

a. **Vasopressin (Pitressin®)**. This agent is used for the control or prevention of the symptoms and complications of diabetes insipidus. For vasopressin injection, the dose is 5 to 10 units (0.25 to 0.5 milliliters) by intramuscular or subcutaneous injection as required (usually every 2 to 3 hours as needed). The side effects associated with this product include abdominal cramps, fluid retention, and increased blood pressure. It is dispensed for hospital use only and should never be administered intravenously. This drug is available as a solution containing 20 pressor units per milliliter.

b. **Lypressin (Diapid®).** This agent is also used for the control or prevention of the symptoms and complications of diabetes insipidus. The usual dosage of this drug is 1 to 2 sprays applied to each nostril four times daily. The side effects associated with lypressin are abdominal cramps, nasal congestion, fluid retention, and increased bowel movements. Lypressin is useful in patients suffering from diabetes insipidus who have become unresponsive to other therapy or who experience allergic or other undesirable reactions to antidiuretic hormone of animal origin. The product has to be kept refrigerated. This product has an expiration date of 36 months. It is available as a nasal spray, 0.185 milligrams of lypressin per milliliter of solution (equivalent to 50 units per milliliter).

Continue with Exercises

EXERCISES, LESSON 8

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. Which of these conditions is treated with diuretics?

   a. Asthma.

   b. Congestive heart failure.

   c. Diabetes mellitus.

   d. Gallstones.

2. Which of the following statements best describes the mechanism of action for the thiazide diuretics?

   a. Thiazide diuretics cause sodium diuresis and potassium retention by acting as an aldosterone competitive antagonist.

   b. Thiazide diuretics produce a diuresis of water by drawing water from the cells in the body and thus by increasing the glomerular filtrate.

   c. Thiazide diuretics work by the inhibition of sodium reabsorption in the first portion of the distal tubule.

   d. Thiazide diuretics inhibit sodium transport--and thus sodium excretion--in the ascending limb of the Loop of Henle, the distal tubule, and in the proximal tubule.

3. Mannitol is used to:

    a. Prevent or treat acute liver failure.

    b. Treat dehydration and electrolyte imbalance.

    c. Promote the excretion of toxic substances in the urine.

    d. Treat epilepsy.

4. Hydrochiorothiazide is used to treat:

    a. Essential hypertension.

    b. Diabetes mellitus.

    c. Hyperglycemia.

    d. Cramping and diarrhea.

5. Vasopressin is used:

    a. For the control or prevention of the symptoms and complications of diabetes insipidus.

    b. To treat hypovolemia.

    c. To treat nasal congestion.

    d. To prevent hyperkalemia.

6. Which of the following is a side effect associated with Dyazide®?

    a. Hypouricemia.

    b. Hyperglycemia.

    c. Hypernatremia.

    d. Fluid retention.

7. Diamox® is used in the treatment of:

   a. Edema because of congestive heart failure.

   b. Drug-induced edema.

   c. Open-angle glaucoma and secondary edema.

   d. All the above.

8. Match the drug name in Column A with its corresponding trade or generic name listed in Column B.

Column A	Column B
____ Aldactazide®.	a. Chlorothiazide.
____ Spironolactone.	b. Aldactone.
____ Furosemide.	c. Combination of spironolactone and hydrochlorothiazide.
____ Diapid®	d. Lypressin.
____ Diuril®.	e. Lasix®
____ Dyrenium®.	f. Triamterene.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 8

1. b (para 8-3)
2. c (para 8-4b)
3. c (para 8-4a(2))
4. a (para 8-4b(1))
5. a (para 8-7a)
6. b (para 8-4g(2))
7. d (para 8-4d(3))
8. c Aldactazide®.(para 8-4b(2))
   b Spironolactone.(para 8-4c(1))
   e Furosemide. (para 8-4g(2))
   d Diapid®. (para 8-7b)
   a Diuril®. (para 8-4e)
   f Dyrenium®. (para 8-4c(2))

a. Chlorothiazide.
b. Aldactone.
c. Combination of spironolactone and hydrochlorothiazide.
d. Lypressin.
e. Lasix®.
f. Triamterene

End of Lesson 8

LESSON ASSIGNMENT

SUBCOURSE MD0806 Therapeutics III.

LESSON 9 Toxicology and Poison Control.

LESSON ASSIGNMENT Paragraphs 9-1--9-13.

LESSON OBJECTIVES After completing this lesson you will be able to:

9-1. Given a list of numbers, select the number of deaths per year which are caused by accidental poisonings.

9-2. Given a list of statements and one of the following terms: poison and toxicology, select the definition of the given term.

9-3. Given a group of statements, select the purpose of the Poison Prevention Packaging Act of 1970.

9-4. From a group of statements, select the requirement(s) of the Poison Prevention Packaging Act of 1970.

9-5. Given a prescription and a list of types of prescription containers, select the type of container that should be used to contain the medication when it is dispensed to the patient.

9-6. Given a group of statements, select the statement(s) that best explain(s) the exceptions to the Poison Prevention Packaging Act of 1970.

9-7. Given a statement pertaining to the treatment of a poisoning victim, select the statement that best describes the best treatment.

9-8. Given a situation involving an accidental poisoning and a list of references, select the reference that would provide the information required by the description of the situation.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 9

TOXICOLOGY AND POISON CONTROL

Section I. INTRODUCTION

9-1. GENERAL

It is estimated that accidental poisonings result in about 4,000 deaths per year, while suicides by chemical agents result in about 6,000 deaths per year in the United States. Each year there are some 500,000 children involved in accidental poisonings. Approximately 90 percent of these poisonings occur in children who are too young to attend school. You have probably read and heard about many cases of accidental poisonings. As a pharmacy technician you may be asked to provide information to professional personnel or to the public in an emergency situation. It is therefore imperative that you be familiar with some general treatment procedures and information sources pertinent to poisoning. Just as important, you can provide guidance which can help persons avoid the tragedy associated with an accidental poisoning.

9-2. DEFINITIONS

a. **Poison**. A poison is any substance which when ingested, inhaled, absorbed, applied, injected, or even manufactured by the organism itself may cause damage to the structure of that organism or destruction to the normal functioning of that organism.

b. **Toxicology**. Toxicology is the scientific study of poisons--their actions, detection, and the treatment of the conditions they produce.

9-3. CAUSES OF POISONING

a. **Intentional**. Individuals for a variety of reasons can intentionally ingest poisons. Some of these reasons are:

(1) To commit suicide.

(2) To gain personal attention.

(3) To commit child abuse.

b. **Accidental**. Accidental poisonings usually affect children. In the years from 1972 through 1976, there were from one to two million cases of accidental poisoning per year in the United States. Since 1976, this number of accidental poisonings has dropped to approximately 500,000 cases per year. This decrease is attributed to the Poison Prevention Packaging Act and to poison prevention publicity. The most common sources of accidental poisoning were plants, various types of cleaners (soaps, detergents, and cleaners), vitamins and minerals, and aspirin. It is interesting to note that aspirin is no longer the most common cause of accidental poisoning (this is probably due to child resistant packaging).

Section II. THE PHARMACY AND POISON PREVENTION

9-4. THE POISON PREVENTION PACKAGING ACT OF 1970

The purpose of the Poison Prevention Packaging Act of 1970 is to reduce poisonings among small children. The Act provides that certain household products (such as aspirin and certain other drugs, including oral prescription drugs; furniture polish; oil of wintergreen, antifreeze; some cleaners for drains and ovens; turpentine; and cigarette lighter fluid), which are found to be hazardous or potentially hazardous must be sold in safety packaging. This safety packaging must be designed so that most children under five years of age cannot open the packages.

9-5. THE REQUIREMENTS OF THE POISON PREVENTION PACKAGING ACT OF 1970

a. The Act requires the previously mentioned products to be packaged in containers which are sufficiently difficult to open in order to prevent 80 percent of children under five years of age from opening them. However, the containers must allow access to at least 90 percent of adults who will be able to open and properly close the packaging conveniently.

b. The Act requires that the prescription filled in the pharmacy--with the exceptions noted in paragraph 9-6 below--be dispensed in child-resistant containers. The requirements below are especially important:

(1) Prescriptions which are not to be refilled. For a prescription that is not to be refilled, the medication must be dispensed in either a glass or a plastic container with a child-resistant top.

(2) Prescriptions which are to be refilled. For a prescription that is to be refilled, the medication must be dispensed in either a glass or a plastic container which has a child-resistant top. If the medication is dispensed in a glass container, a new child-resistant top must be placed on the container whenever the prescription is refilled. If the medication is dispensed in a plastic container, upon refilling, the medication must be placed in a new plastic container with a new child-resistant top. That means that a new label must be prepared for the refill when the medication is placed in a plastic container.

9-6. EXCEPTIONS TO THE ACT

Some patients (that is, those who have arthritis) may find child-resistant packaging too difficult to open. Furthermore, some patients (for example: those with certain types of heart conditions) may wish to obtain their medications from the container in a short period of time when they need them. For these types of patients, alternatives to child--resistant packaging are available.

a. **Nitroglycerin Must NOT be Dispensed in Child--Resistant Packaging.** This drug is for patients who have certain types of heart conditions. These patients must be able to obtain their nitroglycerin quickly in the event they need it.

b. **Alternative Packaging**. The manufacturer can market one size of a product in conventional (not child-resistant) packaging--if the same product is also available in child-resistant packaging. However, the conventional packaging must have a label which clearly states:

This packaging for household without young children.

or if the package is small:

Package not child-resistant.

c. **Patient or Physician Request.** The patient or prescribing physician may request that prescription medicines be put into ordinary packaging without safety features. Although some pharmacists may ask for a written statement from a patient before providing a conventional closure, this is not a requirement of the Federal law.

9-7. CONSIDERATIONS FOR THE OUTPATIENT PHARMACY

Child-resistant packaging has been in use for quite some time. It has, without a doubt, decreased the number of cases of accidental poisonings. If you have purchased items or received prescriptions packaged in child-resistant containers, you are aware of the advantages and disadvantages of this means of preventing accidental poisonings. In your position in the pharmacy, you may hear comments about the packaging. Some patients are quick to complain about the packaging. Here are some considerations about the act that are pertinent to you:

a. You should be very familiar with your pharmacy's policies regarding child-resistant packaging. For example, if a patient requests conventional packaging for a prescription item, does your pharmacy require the patient to sign or initial the prescription or a special form? You should carefully read and study your local standing operating procedures (SOP) to ensure you do what is required.

b. Some patients may request conventional packaging. Suppose a retired individual asks you to package his prescription in a conventional container. Does this person have grandchildren who frequently come to the home? Remember, many poisonings occur when a small child visits grandparents and goes through the medicine cabinet or grandmother's purse.

c. Some pharmacies sponsor poison prevention campaigns. These campaigns focus on the basics of poison prevention. Frequently overlooked basics include keeping materials (cleaners, drugs, insecticides, and so forth) in their original containers and disposing of unused medications. Many persons repackage substances (like insecticides in soft drink bottles) only to tragically discover that a young child has ingested the poison thinking it was something else. Above all, these publicity campaigns seek to make people aware of dangerous practices which could result in tragedy.

Section III. THE TREATMENT OF POISONING

9-8. INTRODUCTION

Suppose a poisoning has occurred. What should be done to treat the patient? Because of your position in the pharmacy you probably will not be called upon to treat persons who are victims of intended or accidental poisoning. You should know the essentials of first aid and you should know to immediately take the victim to medical professionals who have been trained to treat poisoning victims. The information given below is not intended to serve as a strict procedure for the treatment of poisonings. Instead, it is intended to give general guidelines. Remember, the treatment given depends, to a great extent, on the poison ingested, absorbed, or inhaled.

9-9. TREATMENT GUIDELINES FOR POISONING VICTIMS

a. **Screen the Patient**. In the screening process it is important to identify the specific poison affecting the person and how the person was exposed to it. That is, if a child is suffering from poisoning from a particular insecticide (for example, malathion) was the insecticide swallowed or was it absorbed through the skin?

b. **Minimize Absorption**. There are three ways in which the amount of poison absorbed into the patient's system may be decreased.

(1) Remove the poison. The poison, if swallowed, can sometimes be removed by emesis (having the patient to vomit). Depending upon the type of poison ingested, the physician may or may not have the patient to vomit. Syrup of Ipecac and apomorphine are recognized as effective emetics. Emetic agents should not be administered to all patients. Specifically, emetic agents should not be administered to patients who are unconscious or convulsing, to persons who have ingested caustic or corrosive agents, or to patients who have ingested volatile petroleum products. One should not administer sodium bicarbonate ($NaHCO_3$) to a patient who has ingested a substance containing a corrosive agent such as hydrochloric acid (HCl), because the two chemicals might react to form carbon dioxide gas ($HCl + NaHCO_3 \rightarrow NaCl + CO_2(\uparrow) + H_2O$) that could distend or even perforate the stomach.

(2) Administer gastric lavage.

(3) Administer cathartics.

c. **Retard Absorption**. There are two methods by which the absorption of toxins can be retarded.

(1) Dilute the poison. Water, milk, flour or cornstarch suspension can be used to dilute (lower the concentration of) the poison. When the concentration of the poison is lowered, the amount of poison absorbed in a given period of time is usually lower.

(2) Administer activated charcoal. The activated charcoal adsorbs the poison and thereby reduces the amount of the poison which is available for adsorption. It should be noted that if both syrups of ipecac and activated charcoal are to be used, the activated charcoal must not be given until after the ipecac-induced emesis has occurred since the charcoal will render the ipecac ineffective.

d. **Administer Systemic Antidotes (when possible).** As you know, antidotes are substances which counteract the effects of other substances. Unfortunately, not every substance which is a toxin has an antidote which will serve to render its effects harmless. When the physician sees the poisoning victim, he must know what the identity of the ingested poison is before he considers giving an antidote. Furthermore, even after the identify of the poison is known, there must be an antidote in existence for that particular poison. Some examples of antidotes are naloxone (Narcan®), for narcotic poisonings--atropine, for the treatment of certain insecticide poisonings--BAL in Oil, for arsenic, gold, and mercury poisoning--Edetate Calcium Disodium, for lead poisoning--and flumazenil (Romazicon®) for benzodiazepine overdose.

e. **Speed the Elimination of the Poison**. As you might expect the effects of a toxin can be reduced in many instances if that substance is quickly eliminated from the body. Methods such as forced diuresis, through the administration of hypertonic solutions and through adjustment of urine pH; peritoneal dialysis, and hemodialysis (hematodialysis) can be used to speed the elimination of certain poisons from the body.

f. **Support the Patient**. In all poisonings the patient must be supported. That is, the physician must carefully monitor the patient--through observation and by laboratory tests. When required, the physician may administer drugs for pain, replace fluids and electrolytes, regulate body temperature, maintain respiration, and maintain the nutrition of the patient.

Section IV. POISON CONTROL AND INFORMATION

9-10. INTRODUCTION

As with many types of emergencies, the poisoning emergency happens without notice. It is important that information sources pertaining to poisoning be maintained in the pharmacy and at certain other locations (that is, hospital emergency rooms and poison control centers). These sources of information must be up to date. Furthermore, the personnel who work in the area must be trained in the rapid use of these references.

9-11. POISON INFORMATION/CONTROL CENTERS

Poison control/information centers provide ready sources of information concerning poisons and chemical substances. These centers are usually staffed on a 24-hour basis. The Physicians' Desk Reference contains a section entitled "Directory of Poison Control Centers" which states the location and telephone number of poison control centers located in the United States. Regardless of the size of the medical treatment facility or the pharmacy, the number of the closest Poison Control Center should be posted on the wall or telephone where everyone can see the number.

9-12. SUGGESTED REFERENCES TO BE MAINTAINED IN THE PHARMACY IN RELATION TO POISONING INFORMATION

Lesson 1 of MD0804, Therapeutics I, discussed journals and texts pertinent to the practice of pharmacy. In addition to the references listed in that lesson, the pharmacy should maintain, at a minimum, the following references.

a. **Physician's Desk Reference.** This reference contains product information (that is, the ingredients in a particular product). It is indexed so that the information can be found if the manufacturer, trade name, or chemical composition of the product is known. The Product Identification Section of the Physicians' Desk Reference is very helpful in that if a tablet or capsule of the medication is on hand, this section can be used to rapidly identify it in most instances. Also helpful is the "Guide to Management of Drug Overdose" found on the back inside cover.

b**. American Drug Index**. In this text the trade and generic names of the medications are cross-indexed. No specific information on toxicity's is included in this text.

c. **Merck Index**. In this text the trade and generic names of the products are cross--indexed. Foreign as well as American products are included in this text.

d. **Handbook of Poisoning.** This text is organized according to the type of setting in which poisoning might occur (that is, agricultural, industrial, household, plant, insect, and so forth.). The text also presents an excellent discussion of such pertinent topics as poison prevention, emergency treatment, and poisoning diagnosis.

e. **Handbook of Nonprescription Drugs**. This reference identifies the ingredients of over-the-counter products.

f. **Clinical Toxicology of Commercial Products**. This comprehensive text contains information on over 17,000 products and ingredients. It discusses the signs, symptoms, and treatment of various types of poisonings. One caution: It is rather a complex book to use. Therefore, you should acquaint yourself with this text before you have to use it in an emergency situation.

g. **Poisindex©.** Poisindex, as part of the subscription to Micromedex, is available as a quick, thorough reference. Most drug information centers and emergency departments will have Poisindex set up as an icon on their desktop computers for quick reference.

9-13. CONCLUDING COMMENTS

The references just described contain essential information on topics related to poisoning. The quick use of these references to learn of poisoning signs, symptoms, and treatments have saved many a patient's life. Just think, many accidental poisonings can be prevented. The best therapy is that of prevention. You are in a unique position to help the patient realize that they should safeguard their medications in order to prevent any type of accidental poisoning. It is much easier to prevent most poisonings than it is to treat those poisonings. Some pharmacies emphasize poisoning prevention through such programs as the collection of unused medication. You can have your own poisoning prevention program in your own home.

Continue with Exercises

EXERCISES, LESSON 9

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. How many deaths per year are caused by accidental poisonings?

   a. 2,000.

   b. 4,000.

   c. 6,000.

   d. 500,000.

2. The term poison is best defined as:

   a. A chemical which will cause death if it is ingested.

   b. Any substance which will cause destruction of living cells.

   c. Any substance which when ingested, inhaled, absorbed, applied, injected, or even manufactured by the organism itself will cause damage to the organism or will interfere with its normal functioning.

   d. Any substance or chemical which when ingested, inhaled, or in any other way taken into the body, will cause death to the cells of the organism.

3. What is the purpose of the Poison Prevention Packaging Act of 1970?

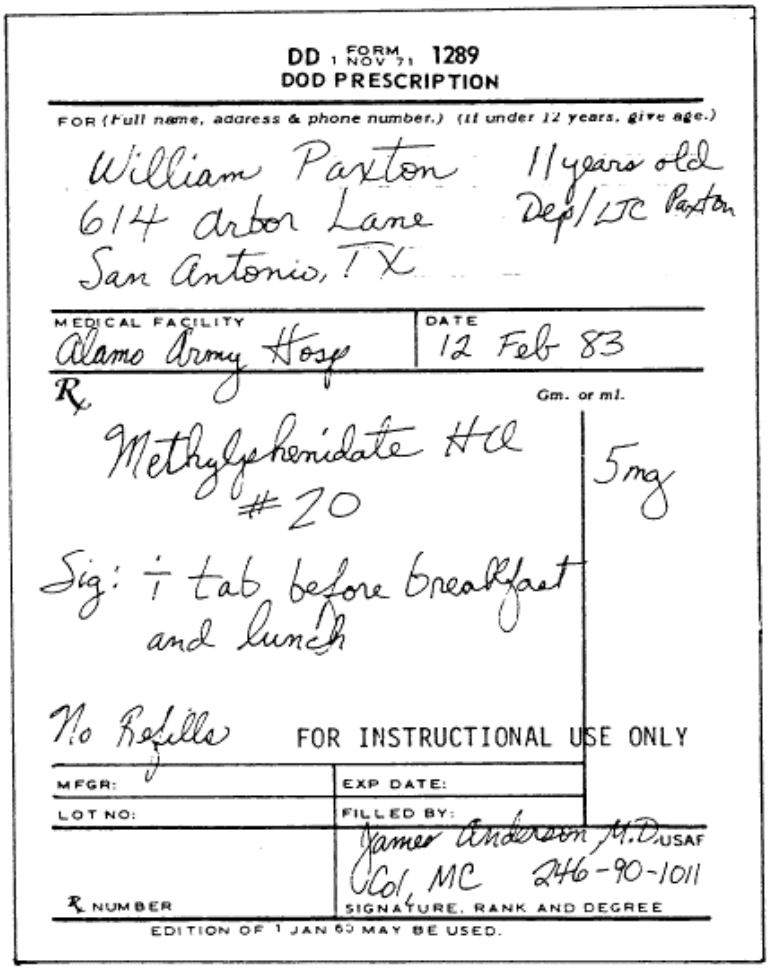
   a. To reduce poisonings among small children.

   b. To reduce the number of intentional poisonings among children and adults.

   c. To reduce the number of accidental deaths caused by aspirin.

   d. To require packaging that could be opened only by children over the age of 13.

4. You are to fill the prescription below. What type of container must be used to dispense the drug to the patient?



DD FORM 1 NOV 71 1289
DOD PRESCRIPTION

FOR (Full name, address & phone number.) (If under 12 years, give age.)
William Paxton 11 years old
614 Arbor Lane Dep/LTC Paxton
San Antonio, TX

MEDICAL FACILITY: Alamo Army Hosp
DATE: 12 Feb 83

℞ Gm. or ml.
Methylphenidate HCl 5mg
#20

Sig: 1 tab before breakfast and lunch

No Refills FOR INSTRUCTIONAL USE ONLY

MFGR:
EXP DATE:
LOT NO:
FILLED BY: James Anderson, M.D. USAF
Col, MC 246-90-1011
℞ NUMBER
SIGNATURE, RANK AND DEGREE

EDITION OF 1 JAN 60 MAY BE USED.

a. A glass container without a child-resistant top.

b. A plastic container without a child-resistant top.

c. A plastic or glass container without a child-resistant top.

d. A glass or plastic container with a child-resistant top.

5. Which of the following statements best explains an exception to the Poison Prevention Packaging Act of 1970?

   a. Aspirin (ASA) must not be dispensed in child-resistant packaging for the convenience of those patients who have arthritis.

   b. Nitroglycerin must not be dispensed in child-resistant packaging.

   c. Federal law requires that patients who desire their medications be dispensed in conventional packaging must sign a disclaimer statement on the back of the prescription form.

   d. Only persons who suffer from heart disease or arthritis may request their medications be dispensed in conventional packaging.

6. You suspect that your two-year-old child has just ingested some poisonous substance. What is the first thing you should do?

   a. Make the child ingest some syrup of ipecac.

   b. Identify the substance to which the child was exposed and how he was exposed to it.

   c. Make the child drink a 5 percent solution of sodium bicarbonate (NaHCO3).

   d. Administer a hypertonic solution intravenously to the child.

7. The Chief, Pharmacy Service, has asked you to prepare a brief report on poison prevention. Which of the following references would you use to prepare the report?

   a. Handbook of Nonprescription Drugs.

   b. Physicians' Desk Reference.

   c. Merck Index.

   d. Handbook of Poisoning.

8. You are asked to find some information on an insecticide not used in the United States. Which of the references below would you use to locate some information on this product?

   a. Clinical Toxicology of Commercial Products.

   b. Handbook of Nonprescription Drugs.

   c. Handbook of Poisoning.

   d. Merck Index.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 9

1. b (para 9-1)
2. c (para 9-2b)
3. a (para 9-4)
4. d (para 9-5b(1))
5. b (para 9-6a)
6. b (para 9-9a)
7. d (para 9-12d)
8. d (para 9-12c)

End of Lesson 9

ANNEX

DRUG PRONUNCIATION GUIDE

This Drug Pronunciation Guide was developed to help you to learn how the trade and generic names of commonly prescribed medications are frequently pronounced. Not all the drugs in the guide are discussed in this subcourse. Remember, it is not enough to be able to know the uses, indications, cautions and warnings, and contraindications for a drug--you must also know how to pronounce that drug's name.

Trade Name	***Generic Name***
A	
Actifed (Ak'-ti-fed)	Triprolidine (Tri-pro'-li-deen) and Pseudoephedrine (Soo-do-e-fed'-rin)
Adapin (Ad'-a-pin)	Doxepin (Dok'-se-pin)
Sinequan (Sin'-a-kwan)	" "
Afrin (Af'-rin)	Oxymetazoline (Ok-see-met-az'-o-leen)
Aldactazide (Al-dak'-ta-zide)	Spironolactone (Spi-ro-no-lak'-tone) and Hydrochlorothiazide (Hy-dro-klor-thi'-a-zide)
Aldactone (Al-dak'-tone)	Spironolactone (Spi-ro-no-lak'-tone)
Aldomet (Al'-do-met)	Methyldopa (Meth-il-do'-pah)
Alupent (Al'-u-pent)	Metaproterenol (Met-a-pro-ter'-eh-nol)
Amoxil (Am-ok'-sil)	Amoxicillin (Ah-moks'-i-sil-in)
Amphojel (Am'-fo-jel)	Aluminum (Al-loo'-mi-num) Hydroxide (Hy-drok'-side)
Ampicillin (Amp'-I-sil-in)	Same
Antepar (Ab'-te-par)	Piperazine (Pi-per'-ah-zeen)
Anturane (An'-tu-rain)	Sulfinpyrazone (Sul-fin-pie'-ra-zone)
Anusol (An'-u-sol)	Pramoxine (Pram-ok'-seen)
Apresoline (A-press'-o-leen)	Hydralazine (Hy-dral'-ah-zeen)
Aralen (Ar'-a-len)	Chloroquine (Klor'-o-kwin)
Aristocort (A-ris'-to-cort)	Triamcinolone (Tri-am-sin'-o-lone)
Artane (Ar'-tane)	Trihexyphenidyl(Tri-hek-see-fen'-i-dil)
A.S.A.	Aspirin (As'-per-in)
Atromid S (A'-tro-mid)	Clofibrate (Klo-fi'-brate)
Avlosulfon (Av-lo-sul'-fon)	Dapsone (Dap'-sone)
Azolid (Az'-o-lid)	Phenylbutazone (Fen-il-bute'-a-zone)
B	
Bactrim (Bak'-trim)	Sulfamethoxazole (Sul-fah-meth-oks'-ah-zole) and Trimethoprim (Tri-meth'-o-prim)
Bellergal (Bel'-er-gal)	Ergotamine (Er-got'-a-meen), Phenobarbital (Feen-o-bar'-bi-tal) and Belladonna (Bel-la-don'-na) Alkaloids

Trade Name	*Generic Name*
Benadryl (Ben'-a-dril)	Diphenhydramine (Di-fen-hy'-dra-meen)
Bendectin (Ben-dek'-tin)	Doxylamine (Dok-sil'-a-meen)
Benemid (Ben'-eh-mid)	Probenecid (Pro-ben'-eh-sid)
Bonine (Bo'-neen)	Meclizine (Mek'-li-zeen)
C	
Cafergot (Kaf'-er-got)	Ergotamine (Er-got'-a-meen) and Caffeine (Kaf'-feen)
Calamine (Kal'-a-mine)	Same
Catapres (Kat'-a-press)	Clonidine (Klo'-ni-deen)
CeeNu (See'-new)	Lomustine (Lo-mus'-teen)
Chlor-Trimeton (Klo-tri '-meh-ton)	Chlorpheniramine (Klor-fen-it'-a-meen)
Clomid (Klo'-mid)	Clomiphene (Klo'-mi-feen)
Clonopin (Klo-o-pin)	Clonazepam (Klo-na'-ze-pam)
Codeine (Ko'-deen)	Same
Cogentin (Ko-jen'-tin)	Benztropine (Benz'-tro-peen)
Colace (Ko'-lace)	Dioctyl(Di-ok'-til) Sodium (So'-dee-um) Sulfosuccinate (Sul-fo-suk'-si-nate)
Colchicine (Kol'-chi-seen)	Same
Compazine (Kom'-pa-zeen)	Prochiorperazine (Pro-klor-per'-a-zeen)
Cordran (Kor'-dran)	Flurandrenolide (Floor-an-dren'-o-lide)
Coumadin (Koo'-mah-din)	Warfarin (War'-fah-rin)
CP	Cloroquine (Klor'-o-kwin) and Primaquine (Prim'-a-kwin)
Cyclogyl (Si'-klo-jel)	Cyclopentolate (Si-klo-pen'-to-late)
Cytomel (Si'-to-mel)	Liothyronine (Li-o-thy-ro-neen)
Cytoxan (Si-tok'-san)	Cyclophosphamide (Si-klo-fos'-fa-mide)
D	
Dalmane (Dal '-mane)	Flurazepam (Floor-az'-e-pam)
Darvocet (Dar'-vo-set)	Propoxyphene (Pro-pok'-se-feen) and Acetaminopen (As-et-am'-ino-fen)
Darvon (Dar'-von)	Propoxyphene (Pro-pok-se-feen)
Decadron (Dek'-a-dron)	Dexamethasone (Dek-sa-meth'-ah-sone)
Deltasone (Del '-ta-sone)	Prednisone (Pred'-ni-sone)
Demerol (Dem'-er-ol)	Meperidine (Meh-pair'-i-deen)
Dexedrine (Deks '-eh-dreen)	Dextroamphetamine (Deks-tro-am-fet'-a-meen)
Diabinese (Di-ab'-i-nees)	Chlorpropamide (Klor-prop'-a-mide)
Diethylstilbestrol (Di-eth-il-stil-bes'-trol)	Same
Dilantin (Di-lan'-tin)	Phenytoin (Fen'-i-toin)
Dilaudid (Di-law'-did)	Hydromorphone (Hy-dro-more' -fon)
Dimetane (Di'-meh-tane)	Brompheniramine (Brom-fen-ir'-a-meen)

Trade Name	*Generic Name*
Dimetapp (Di‘-meh-tap)	Brompheniramine (Brom-fen-ir’-a-meen) Phenylephrine (Fen-il-ef’-rin) and Phenylpropanolamine (Fen-il-pro-pan-ol‘-a-meen)
Disophrol (Dice’-o-frol)	Dexbrompheniramine (Deks-brom-fen-ir‘-a-meen) and Pseudoephedrine (Soo-do-e-fed‘-rin)
Dolophine (Dol‘-o-feen)	Methadone (Meth’-a-done)
Domeboro (Dome-bor’-o)	Aluminum (Ah-loo’-mi-num) Acetate (As‘-e-tate)
Donnatal (Don’-na-tal)	Belladonna (Bel-la-don’-na) Alkaloids (Al’-ka-loids) and Phenobarbital (Feen-o-barb’-i-tal)
Doxidan (Dok’-si-dan)	Danthron (Dan’-thron) and Dicctyl (Di-ok’-til) Calcium (Kal‘-see-um) Sulfosuccinate (Sul-fo-suk’-si-nate)
Drixoral (Driks’-or-al)	Dexbrompheniramine (Deks-brom-fen-ir’-a-meen) and Pseudoephedrine (Soo-do-e-fed‘-rin)
Dulcolax (Dul’-ko-laks)	Bisacodyl (Bis-a’-ko-dil)
Dyazine (Di’-a-zide)	Triamterene (Tri-am’-ter-een) and Hydrochlorothiazide (Hy-dro-klor-o-thi‘-a-zide)
Dymelor (Die’-meh-lor)	Acetohexamide (As-e-to-heks’-a-mide)
Dyrenium (Die-ren’-i-um)	Triamterene (Tri-am’-ter-een)
E	
Efudex (Ef'-u-deks)	Fluorouracil (Floo-ro-ur’-ah-sil)
Elavil (El’-ah-vil)	Amitriptyline (Am-i-trip’-til-een)
Elixir Terpin (Ter’-pin) Hydrate	Same
Empirin (Em’-per-in)	Codeine (Ko’-deen) and Aspirin (As’-per-in)
E-Mycin (E-mie’-sin)	Erythromycin (E-rith-ro-mie’-sin)
Equanil (Ek’-wa-nil)	Meprobamate (Me-pro-bam’-ate)
Ergomar (Er’-go-mar)	Ergotamine (Er-got’-a-meen)
Ergotrate (Er’-go-trate)	Ergonovine (Er-go-no’-veen)
Erythrocin (Er-eeth’-ro-sin)	Erythromycin (Er-eeth-ro-my’-sin) Stearate (Stare’-rate)
Esidrix (Es’-i-driks)	Hyrochlorothiazide (Hy-dro-klor-o-thi‘-a-zide)
F	
Feosol (Fe’-o-sol)	Ferrous (Fer’-rus) Sulfate (Sul’-fate)
Fergon (Fer’-gon)	Ferrous (Fer’-rus) Gluconate (Glu'-con-ate)

Trade Name	*Generic Name*
Fiorinal (Fee-or'-i-nal)	Butalbi tal (Bu-tal'-bi-tal), Apririn, Phenacetin (Fen-ass'-eh-tin), and Caffeine (Kaf'-feen)
Flagyl (Fla'-jil)	Metronidazole (Me-tro-ni'-dah-zole)
Flexeril (Flek'-sa-ril)	Cyclobenzaprine (Si-klo-benz'-a-preen)
Fulvicin (Ful'-vi-sin)	Griseofulvin (Griz-e-o-ful'-vin)
G	
Guantanol (Gan'-ta-nol)	Suiphamethoxazole (Sul-fah-meth-oks'-ah-zole)
Gantrisin (Gan'-tri-sin)	Sulfisoxazole (Sul-fi-sok'-sah-zole)
Gelusil (Jel'-u-sil)	Aluminum (Ah-loo'-mi-num) Hydroxide (Hy-drok'-side) and Magnesium (Mag-nee'-zee-um) Hydroxide
Grifulvin (Gri-ful'-vin)	Griseofulvin (Griz-e-o-ful'-vin)
Gynergen (Jin'-er-jen)	Ergotamine (Er-got'-a-meen)
H	
Haldol (Hal'-dol)	Haloperidol (Hal-o-pair'-i-dol)
Halotestin (Hal-o-tes'-tin)	Fluoxymesterone (Floo-ok-see-mes-teh-rone)
Hexadrol (Hek'-sa-drol)	Dexamethasone (Dek-sa-meth'-a-sone)
Hydrodiuril (Hy-dro-di'-ur-il)	Hydroclorothiazide (Hy-dro-kior-thi'-a-zide)
Hygroton (Hy-grow'-ton)	Chiorthalidone (Kior-thal'-i-done)
I	
Ilosone (I'-low-sone)	Erythromycin (Er-ith-ro-mi'-sin) Estolate (Es'-to-late)
Inderal (In'-der-al)	Propranolol (Pro-pran'-o-lol)
Indocin (In'-do-sin)	Indomethacin (In-do-meth'-a-sin)
INH	Isoniazid (I-so-ni'-a-zid)
Insulin (In'-sul-in)	Same
Intal	Cromolyn (Kro'-mo-lin)
Ismelin (Is'-meh-lin)	Guanethidine (Gwan-eth'-i-dine)
Isopto-Atropine (I-sop-to-at'-ro-peen)	Atropine (At'-ro-peen)
Isopto-Carpine (I-sop-to-car'-peen)	Pilocarpine (Pile-o-car'-peen)
Isordil (I'-sor-dil)	Isosorbide (I-so-sor'-bide)
J-K	
Keflex (Kef'-lex)	Cephalexin (Sef-ah-lek'-sin)
L	
Lanoxin (Lan-ok'-sin)	Digoxin (Di-jok'-sin)
Larodopa (Lar-o-do'-pa)	Levodopa (Le-o-do'-pa)
Larotid (Lar'-o-tid)	Amoxicillin (Ah-moks'-i-sil-in)
Lasix (La'-siks)	Furosemide (Fu-ro'-se-mide)
Leukeran (Lu'-ker-an)	Chlorambucil (Klor-ram'-bu-sil)

Trade Name	*Generic Name*
Librium (Lib'-ree-um)	Chlordiazepoxide (Klor-die-az-eh-pok'-side)
Lidex (Lie'-deks)	Fluocinoide (Floo-o-sin'-o-nide)
Lomotil (Lo'-mo-til)	Diphenoxylate (Die-fen-ok'-si-late)
Lopressor (Lo'-pres-sor)	Metoprolol (Met-o-pro'-lol)
Lotrimin (Lo'-tri-min)	Chlotrimazole (Klo-trim'-ah-zole)
M	
Maalox (May'-loks)	Aluminum (Ah-loo'-mi-num) and Magnesium (Mag-nee'-zee-um) Hydroxides
Macrodanton (Ma-kro-dan'-tin)	Nitrofurantoin (Ni-tro-fur-an'-toin)
Mandelamine (Man-del'-a-meen)	Methenamine (Meth-en'-a-meen) Mandelate (Man'-deh-late)
Medihaler-Iso (Med-i-hail-er-I'-so)	Isoproterenol (I-so-pro-ter'-en-ol)
Mellaril (Mel'-la-ril)	Thioridazine (Thi-o-rid'-a-zeen)
Metamucil (Met-a-mu'-sil)	Psyllium (Sil'-e-um)
Metaprel (Meh'-ta-prel)	Metaproterenol (Meh'-ta-pro-ter'-eh-nol)
Methotrexate (Meth-o-treks'-ate)	Amethopterin (Ah-meth-op'-ter-in)
Milk of Magnesia	Same
Minipress (Min'-i-press)	Prazosin (Pra'-zo-sin)
Minocin (Min'-o-sin)	Minocycline (Mi-no-si'-kleen)
Monistat (Mon'-i-stat)	Miconazole (Mi-kon'-ah-zole)
Motrin (Mo'-trin)	Ibuprofen (I-bu'-pro-fen)
Myambutol (My-am'-bu-tol)	Ethambutol (Eth-am'-bu-tol)
Mycostatin (My-co-stat'-in)	Nystatin (Ny-stat'-in)
Mylanta (My-lan'-ta)	Aluminum (Ah-loo'-mi-num) and Magnesium (Mag-nee'-zee-um) Hydroxides and Simethicone (Si-meth'-i-kone)
Myleran (My-ler-an)	Busulfan (Bu-sul'-fan)
Mylicon (My'-li-kon)	Simethicone (Si-meth'-i-kone)
Mysoline (My'-so-leen)	Primidone (Pri'-mi-done)
N	
Nalfon (Nal'-fon)	Fenoprofen (Fen-o-pro'-fen)
Naprosyn (Na'-pro-sin)	Naproxen (Na-prok'-sen)
Nembutal (Nem'-bu-tal)	Pentobarbital (Pen-to-barb'-i-tal)
Neosynephrine (Nee-o-sin-eh'-frin)	Phenylephrine (Fen-il-eh'-frin)
Nitrobid (Ni'-tro-bid)	Nitroglycerin (Ni-tro-gli'-ser-in)
Nitrol (Ni'-trol)	"
Nitrostat (Ni-tro-stat)	"
Noctec (Nok'-tek)	Chloral Hydrate (Klor'-al- Hy'-drate)
Norfiex (Nor'-fleks)	Orphenadrine Citrate (Or-fen'-a-dreen)
Norpace (Nor'-pace)	Disopyramide (Di-so-peer'-a-mide)

Trade Name	*Generic Name*
Novahistine (No-va-his'-teen) Expectorant	Guaifenesin (Gwi-fen'-eh-sin), Phenylpropanolamine (Fen-il-pro-pan-ol'-a-meen), and Codeine (Ko'-deen)
NTG	Nitroclycerin (Ni-tro-gli'-ser-in)
Nupercainal (New-per-kain'-al)	Dibucaine (Die'-bu-kain)
O	
Oretic (O-ret'-ik)	Hydrochiorothiazide (Hy-dro-kior-thi'-a-zide)
Orinase (Or'-in-ase)	Tolbutamide (Tol-bu'-tah-mide)
Ornade (Or'-nade)	Chlorpheniramine (Klor-fen-ir'-a-meen), Triprolidine (Tri-pro-li-deen) and Pseudoephedrine (Su-do-eh-fed'-rin)
P	
Parafon Forte (Pair'-a-fon For'-tay)	Chlorzoxazone (Klor-zok'-sa-zone)
Percodan (Per'-ko-dan)	Oxycodone (Ok-si-ko'-done)
Periactin (Per-ee-ak'-tin)	Cyproheptadine (Si-pro-hep'-tah-deen)
Persantine (Per-san'-teen)	Dipyridamole (Di-pi-rid'-ah-mole)
Phenobarbital (Feen-o-barb'-it-al)	Same
Phenylpropanolamine (Fen-il-pro-pan-ol'-a-meen)	Same
Pitocin (Pi-tow'-sin)	Oxytocin (Ok-see-tow'-sin)
Pontocaine (Pon'-to-kain)	Tetracaine (Teh'-tra-kain)
Povan (Po'-van)	Pyrvinium (Pire-vin'-ee-um)
Premarin (Prem'-ar-in)	Conjugated (Kon'-joo-gay-ted) Estrogens (Es-tro-jens)
Presamine (Press'-a-meen)	Imipramine (Im-ip'-rah-meen)
Primaquine (Pri'-mah-kwin)	Same
Probanthine (Pro-ban'-theen)	Propantheline (Pro-pan'-the-leen)
Pronestyl (Pro-nes'-til)	Procainamide (Pro-kain'-a-mide)
Prophylthiouracil (Pro-pil-thi-o-u'-rah-sil)	Same
Prostaphlin (Pro-staff'-lin)	Oxacillin (Oks'-ah-sil-in)
Provera (Pro-ver'-ah)	Medroxyprogesterone (Med-rok-see-pro-jes'-ter-one)
Pyridium (Pie-rid'-ee-um)	Phenazopyridine (Fen-ahs-o-per'-i-deen)
Q	
Quinidine (Kwin'-i-deen)	Same
Quinine (Kwie'-nine)	Same
R	
Reserpine (Ree-ser'-peen)	Same
Retin A (Reh'-tin A)	Tretinoin (Tret'-i-noin)
Rifadin (Rie-fad'-in)	Rifampin (Rie-fam'-pin)
Riopan (Rie'-o-pan)	Magaidrate (Mag'-al-drate)

Trade Name	*Generic Name*
Rimactane (Rim-act'-ane)	Rifampin (Rie-fam'-pin)
Ritalin (Rit'-a-lin)	Methylphenidate (Meth-il-fen'-i-date)
Robaxin (Ro-bak'-sin)	Methocarbamol (Meth-o-kar'-ba-mol)
Robitussin (Row-i-tus'-sin)	Guaifenesin (Gwie-fen'-eh-sin)
Robitussin DM	Guiafenesin and Dextromethorphan (Dek-tro-meh-or'-fan)
S	
Sansert (San'-sert)	Methysergide (Meth-ee-ser'-jide)
Seconal (Sek'-o-nal)	Secobarbital (Sek-o-bar'-bi-tal)
Selsun (Sel'-sun)	Selenium (Se-leh'-nee-um)
Septra (Sep'-tra)	Sulfamethoxazole (Sul-fah-meth-oks'-a-zole) and Trimethroprim (Tri-meth'-o-prim)
Serax (See'-raks)	Oxazepam (Oks-az'-eh-pam)
Silvadene (Sil'-va-deen)	Silver Sulfadiazine (Sul-fa-die'-a-zeen)
Sinemet (Si'-ne-met)	Levodopa (Le-vo-do'-pa)
Sinequan (Sin'-a-kwan)	Doxepin (Dok'-seh-pin)
Sorbitrate (Sor'-bi-trate)	Isosorbide (I-so-sor'-bide)
Stelazine (Stel'-a-zeen)	Trifluoperazine(Tri-floo-o-per'-a-zeen)
Sudafed (Soo'-da-fed)	Pseudophedrine (Soo-do-eh-feh'-drin)
Sulamyd (Sul'-a-mid)	Sulfacetamide (Sul-fah-set'-a-mide)
Sulfamylon (Sul-fa-mie'-lon)	Mafenide (Maf'-eh-nide)
Sultrin (Sul'-trin)	Sulfathiazole (Sul-fah-thi'-ah-zole) Sulfacetamide (Sul-fah-set'-ah-mide) and Sulfabenzamide (Sul-fah-benz'-ah-mide)
Surfak (Sur'-fak)	Dioctyl (Di-ok'-til) Calcium (Kal'-see-um) Sulfosuccinate (Sul-fo-suk'-si-nate)
Synalar (Sine'-a-lar)	Fluocinolone (Floo-o-sin'-o-lone)
Synthroid (Sin'-throid)	Levothyroxine (Lee-vo-thi-rok'-sin)
T	
Tace (Tace)	Chlorotrianisene (Klor-o-tri-an'-I-seen)
Tagamet (Tag'-a-met)	Cimetidine (Si-met'-i-deen)
Talwin (Tal'-win)	Pentazocine (Pen-taz'-o-seen)
Tandearil (Tan'-da-ril)	Oxyphenbutazone (Ok-see-fen-bute'-a-zone)
Tegretol (Teg'-reh-tol)	Carbamazepine (Kar-ba-maz'-eh-peen)
Tessalon (Tess'-a-lon)	Benzonatate (Benz-on'-a-tate)
Tetracycline (Tet-ra-si'-kleen)	
Thorazine (Thor'-a-zeen)	Chlorpromazine (Klor-pro'-ma-zeen)
Thyroid (Thy'-roid)	Same
Tigan (Tie'-gan)	Trimethobenzamide (Tri-meth-o-benz'-a-mide)
Timoptic (Tim-op'-tic)	Timilol (Tim'-o-lol)

Trade Name	*Generic Name*
Tinactin (Tin-act'-in)	Tolnaftate (Tol-naf'-tate)
Titralac (Ti'-tra-lak)	Calcium (Kal-see-um) Carbonate (Kar'-bon-ate) and Glycine (Gly'-seen)
Tofranil (Toe'-fra-nil)	Imipramine (I-mip'-rah-meen)
Tolectin (Tow-lek'-tin)	Tolmetin (Tol-met'-in)
Triavil (Tri'-a-vil)	Perphenazine (Per-fen'-a-zeen) and Amitriptlyline (Am-i-trip'-ti-leen)
Trilafon (Try'-la-fon)	Perphenazine (Per-fen-a-zeen)
Tylenol (Tie'-leh-nol)	Acetaminophen (As-et-am'-ino-fen)
Tylenol #3	Acetaminophen and Codeine (Ko'-deen)
U	
Unipen (U'-ni-pen)	Nafcillin (Naf-sil-lin)
Urecholine (Ur-eh-ko'-leen)	Bethanecol (Beth-an'-eh-kol)
V	
Valisone (Val'-i-sone)	Betamethasone (Beh-tah-meth'-a-sone)
Valium (Val'-ee-um)	Diazepam (Die-aze-eh-pam)
Vermox (Ver'-moks)	Mebendazole (Meh-ben'-dah-zole)
Vibramycin (Vie-bra-my'-sin)	Doxycycline (Doks-see-si'-kleen)
W-X	
Xylocaine (Zie'-low-kain)	Lidocaine (Lie-do-kain)
Y-Z	
Zarontin (Zar-on'-tin)	Ethosuximide (Eh-tho-suks'-a-mide)
Zyloprim (Zie'-low-prim)	Allopurinol (Al-lo-pure'-in-ol)

End of Annex